X-RAY PRODUCED MUTATIONS, DELETIONS, AND MOSAICS IN *DROSOPHILA VIRILIS*

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X-RAY PRODUCED MUTATIONS, DELETIONS, AND MOSAICS IN *DROSOPHILA VIRILIS*

DISSERTATION

Presented to the Faculty of the Graduate School of
The University of Texas in Partial Fulfillment
of the Requirements

For the Degree of

DOCTOR OF PHILOSOPHY

By

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Austin, Texas
June, 1948

PREFACE

This investigation was undertaken at the suggestion of Dr. W. S. Stone. Grateful acknowledgement is made to him for his help in planning this work and for the many helpful suggestions which aided in its completion. Acknowledgement is also made to all persons whose names appear on the title-fly page for their constructive criticism of the manuscript.

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April, 1948

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INTRODUCTION

For many years geneticists have held the view that mutations are building blocks of evolution. The extreme rarity with which they were found, however, made it difficult to make quantitative studies on the frequency with which they occur or to offer any substantual evidence that they play an important role in the formation of species.

With the discovery of the effectiveness of X-rays in the production of mutations by Muller (1927), great advances were made possible. Patterson and Muller (1930) showed that different allels of white are produced with different frequencies. Timofeeff-Ressovsky (1932) found a difference in the mutation rate to white of the normal allel in an American stock and a Russian stock of Drosophila melanogaster which was due to the properties of the American and Russian normal allels, and not due to a physiological difference of the stocks. He also studied the rate of production of sex linked lethals in melanogaster as compared with funebris. Koller and Ahmed (1942) have compared the rate of lethal mutations in pseudo-obscura and melanogaster.

These works show that the genes at different loci mutate at various frequencies, but at definite rates for

each locus depending upon the allel present, and that the general mutation rates, as measured by the production of lethal mutations, vary in different species and different stocks from various geographic localities. Two other lines of investigation indicate that different species may not vary greatly either in the total number of genes or the different genes which they possess. Investigations have been made by numerous workers on the homologies of genes and chromosome elements in different species, and on the cytological and genetic studies of hybrids between species within the different groups of Drosophila.

It would be of interest to know more about the homologous genes which are present in two species of different morphological appearance. The normal allels are known primarily through their mutations. Thus, the normal allels of white or singed are known in two species only after they have mutated so that they may be studied, but we do not know that they mutated from an identical "normal" allel. Indications that the "normal" allels are different have been given in the case of the American and Russian allels of white which mutate at different frequencies, in a general manner by the different frequencies of lethal production in various species, and by work done with plants, particularly corn.

The work outlined in this paper has been undertaken

to obtain the frequencies at which mutations, deletions, and other chromosomal changes occur in Drosophila virilis so that they may be compared to Drosophila melanogaster. The experiment has been planned so that visible changes at seven particular loci, which Sturtevant and Novitski (1941) consider to be homologous, can be observed and, thus, make possible a comparison of the rate of changes between the so called "normal" allels for these particular loci in the two species.

MATERIALS

All stocks used were Drosophila virilis which are maintained in the genetics laboratory at the University of Texas. The normal wild type stock that was irradiated was Drosophila virilis Sturtevant, known as Pasadena, which was obtained from Dr. W. P. Spencer of Wooster, Ohio, several years ago.

The two recessive mutant stocks, only one of which included white, contained eight recessive mutants, with their loci, as follows: yellow (y^{40a}) at 2.9, echinus (ec) at 8.7, cross-veinless (cv) at 25.0, vermilion (v^{40d}) at 25.5, singed (si^{2}) at 50.0, dusky (dy) at 78.1, apricot (ap^{40e}) at 136.0, and white (w) at 105.0. During the course of this investigation one of the stocks was either contaminated or some of the mutants reverted to wild type. This was noted immediately in the F_1 males and allowances were made in the F_1 female counts (table 2) so that no inaccuracies resulted.

The same stocks were used throughout the investigation covering a period of about one year. All flies used were taken from bottles which had been spread to insure large, well developed flies.

A Victor X-ray machine with an air-cooled Coolidge tube was used, set at 50 KVP and 10 MA with a one mm.

aluminum filter. A Victoreen r meter was used and a temperature correction applied to determine the Roentgen units discharged per minute both immediately before irradiating the flies and again just after completion of irradiation. The readings varied between 86 and 91 r units per minute. The length of time for each irradiation was calculated on the bases of the first reading. The readings varied between 3010 and 3062 r units. The average dosage was 3047 r units.

Fig. I shows the apparatus used to cool the flies during irradiation. It consisted of a 3 gallon can which would just fit between the two braces holding the X-ray tube so that the same position was obtained each time. In the center of the can a support from the bottom held a smaller can with a side arm used to insert the Roentgen meter and thermometer. The large can was filled about two-thirds full of ice cubes and then filled with water and covered with the top which had a hole in the center. The flies were put in a basket made of a cardboard ring with the bottom made of cheesecloth. The basket was put in the small can, the top of which touched the aluminum filter. The small can was constantly surrounded by ice cubes which floated at the top of the water. In this way it was possible to obtain the same position for the flies in relation to the X-ray tube's target and

also to maintain a constant temperature of from 0.5 to 1.5 degrees Centigrade during the thirty to forty minutes it took to obtain the required dosage, in spite of the heat produced by the tube. The etherized flies were placed in the basket, and due to the low temperature, no covering was needed to prevent their escape. No harmful effect from the temperature was apparent as they were flying around in the bottles within thirty to sixty seconds after removal from the cooling apparatus. Matings were observed within two minutes after removal.

All matings were made either in half pint bottles or vials using standard laboratory food, and except for the time during the X-ray treatment, the flies were kept at a constant temperature of 22 to 23 degrees Centigrade.

METHOD

In order to determine the rates for the various chromosomal alterations, wild type Drosophila virilis males were taken from bottles when they were not more than thirty hours old, aged for eight days, etherized, X-rayed, and mated immediately to virgin females of the recessive mutant stocks which had also been aged eight days. Approximately one hundred to one hundred and fifty females and fifty to one hundred males were mated in each bottle. After two days the flies were transferred to new bottles and again transferred on the fourth day. At the end of the fifth day they were discarded. It is assumed that in five days, during which the males and females were together, all of the sperm which resulted in offspring had been mature at the time of irradiation. A check was made to test this assumption by dating the bottles when mated and by recording the results of the F_1 females from each set separately. (table 1). The results from the F_1 females from each class, which were taken from five separate matings, clearly indicated that the offspring produced on the fifth day of mating contained approximately the same number of affected chromosomes as did the F_1 females produced during the first two days, or the third and fourth days.

A total of about 14,000 wild type males were exposed to irradiation (approximately 3,050 r units) and mated to approximately 21,000 virgin females homozygous for the mutants y ec cv v si dy ap and approximately 5000 virgin females homozygous for y ec cv v si dy w ap; there were fifty separate series over a period of one year. The relatively small number of F_1 females, 83,949, from 14,000 males and 26,000 females is due to three causes: (1) the lethal effect of irradiation on the sperm, (2) the very apparent decreased viability of the marked stock which was used, and (3) the fact that the females were allowed to lay eggs for only five days after mating.

The offspring (F_1) from these matings were examined each day or at least within two days so that any mutant flies found would be virgin. All of the flies were examined for distinct dominant mutations or mutations of the marked loci, non-disjunction, mosaics, gynandromorphs, and mottles, and the females were counted. A total of 589 F_1 flies were saved as possible mutants and mated to one or the other of the parent stocks for further examination, the rest being discarded. Very few of the F_1 "possible mutants" bred true; those that did are discussed later. The F_1 females showing the "marker genes" and the non-disjunction males are tabulated in tables 2 and 3.

The F_1 females showing the phenotype of one of the

marker recessive mutations were backcrossed to the recessive mutant stock in order to differentiate between mutations and deletions, or mutations and lethal effects. This determination was based upon egg counts, cytological study of the salivary chromosomes, and analysis of crossover counts. All three methods were not used in each case. In most instances the F_2 females phenotypically like their mothers, that is all wild type except for the locus in question, were mated a second time to check the conclusions. If the ratio of females to males which showed the wild type gene on either side of the mutant gene in question was approximately 1 to 1, the case was classified as a mutant. If the ratio was twice as many or more females than males (depending upon the double crossover frequency expected or single crossing-over for y, ap, and w) the case was classified as a deletion or mutation with lethal effects in the male. The results are given in table 2.

No specific control was run, but a check on the parent stocks was provided when males and virgins were taken. Only one recessive sex linked eye color mutation was found in the 14,000 males used. Actually many additional males were observed from the same stock during this period.

RESULTS

The experimental results obtained are listed in tables 2, 3, and 4 and will be discussed under the following headings.

Mutations and deletions are discussed for each locus. The cases in which F_1 females showed the recessive marker mutations are divided into three classes based on the results of backcrosses. Those in which the induced mutation is viable in the males are considered viable point mutations. Those cases that did not produce males with the induced mutation are considered to be either deletions or lethal mutations. The test used would not detect a difference in a deletion of a small region of the chromosome, a lethal mutation, and a viable mutation close to a lethal mutation. The third class is composed of all undetermined cases.

Mosaic. This term is limited to flies which show several recessive genes from the female parent. The effects are not visible in all parts of the body and the variegated patterns are not inheritable.

Gynandromorphs. All these sex mosaics resulted from the loss of the paternal X from the male tissue. Diagrams of both the mosaics and gynandromorphs are included in the

appendix.

A Mottled fly is discussed that exhibits variegations of a recessive, heterozygous trait. The variegated pattern is inherited.

Sections are also included on Hyperploid and Non-Disjunction individuals, a group of Special Cases which occur too infrequently to be classified as separate groups, and a list of Mutations.

Table 2 gives the total number of F_1 females which were heterozygous for each of the seven marked loci and the corresponding treated loci. The numbers vary because two different marked stocks were used and because one of the stocks became heterozygous for some of the mutants during the course of the experiment, as explained in the section on materials. Because all of the wild type males were treated exactly the same and mated to untreated females, the results from both stocks are comparable and can be combined into one table.

Both of the mutant stocks contained the mutation echinus, but due to the high frequency of occurrence of rough-eyed flies this gene could not be followed accurately. (From some bottles as many as 10 percent showed some degree of roughness). A great many of these rough-eyed flies showed some degree of dominance in a small percent of their offspring for one to five generations. Others were

stable in their dominant effect, but would not live homozygous. After the first few months of this work, the rough-eyed flies were disregarded because of the labor required to handle the large numbers found.

In all cases given in table 2 in which the F_1 females showed one of the mutant genes, all individuals of succeeding generations from backcrosses also showed the same mutant. This is not always true of the cases listed in tables 3 and 4 which include gynandromorphs and mosaics. Also crossing-over was normal in all cases except for one F_1 female showing ap. However, a large number of the individuals either died shortly after hatching from the pupa, were sterile, or produced so few offspring that cross-over counts were not accurate.

MUTATIONS AND DELETIONS

Each locus gave characteristic results in its rates of mutation, deletion or lethal rate, and in fertility of visible changes.

Yellow locus. Of the thirteen females that showed yellow only one failed to produce offspring. In this case the fly stuck to the food so that it is quite possible that she was capable of laying fertile, viable eggs.

Three of the thirteen flies contained allels of yellow different from the y^{40a} used in the parent stock. One was about the coloration of y^{1}, the other two were only slightly tinged with yellow. Others may have been overlooked as crowded conditions often produce the same appearance. While it is possible that a number of similar allels were missed, many flies were isolated and tested and the two reported are the only ones which bred true. These cases are described later in the list of mutations.

Cross-veinless. Of the nine cross-veinless F_1 females, five produced no offspring or too few to be significant. Three were deletions and one a mutation. Three of those which were undetermined and two of the deletions included both cv and v. Of the two which did produce offspring only small F_2 cultures were obtained. There were five other cases of F_1 females which appeared cross-veinless

but did not breed true. These cases were not included in table 2. Perhaps, some of the five cases which did not produce F_2 offspring should not be counted as cross-veinless.

Vermilion locus. Of the twelve F_1 females which showed vermilion, three failed to produce offspring and five showed both vermilion and cross-veinless. It seems very probable that all those showing both vermilion and cross-veinless were deletions, but two of these died and a third produced only seven offspring and were classed as undetermined. The other six cases were mutations, of which one appeared to give the same phenotype as y^{40d} and the other five gave a new, brighter, and more orange phenotype and also an interaction with apricot unlike y^{40d} which gives no interaction.

Singed locus. The singed locus was affected most frequently of all loci studied. A total of fifty-six F_1 females were found which were completely singed. Some appeared to be more severely affected than others, but this may not have been significant as some variation occurs in the homozygous parent stock. However, none of those marked "extreme singed" produced offspring, and there may have been a different allel or a deletion which caused a more pronounced effect. Twenty-three failed to produce any offspring. In many cases the females died

within one to three days after hatching from the pupae. Others lived for varying lengths of time up to thirty-nine days. These usually laid only a few eggs. Four of the females did lay fertile eggs, but too few individuals were produced in the F_2 or F_3 generations to classify them. Following generations also produced very meager broods and were soon lost. These had to be included in the undetermined group.

Of the twenty-nine F_1 females which produced viable offspring sixteen were mutations and thirteen appeared to be deletions. Neither the mutations nor the heterozygous deletions could be distinguished from the singed used in the parent stock except that several of both classes still produced relatively few offspring after several generations. This reduced fecundity, of course, need not necessarily have been due to the singed locus.

Dusky locus. The dusky locus presented a special problem which possibly led to inaccuracies. Numerous F_1 flies had wings considerably shorter than normal, but did not have the characteristic dusky coloration. These were labeled "possible dy" and backcrossed. They consistently gave normal wings. Because all which did give offspring were not allels of dusky, it seems probable that the identification was not significantly in error, and they were not included in the tabulation of dusky cases.

Four deletions, five mutations, and seven undetermined cases were found for this locus. All appeared the same as the dusky used in the parent stock. There is considerable variation in the wing length of the parent stock of dusky as well as in those found. It is possible that deletions or different allels were responsible for the variation, but this is not apparent.

White locus. The white locus furnished eight F_1 females all of which produced offspring. Of these, seven acted as mutations and one was a deletion which was later confirmed by salivary examination. Only twenty-thousand females were examined for the white locus which is considerably fewer than for the other loci, yet the results for white can be safely compared to the other results in table 2. All of these individuals had white eyes which were not detectably different from the white used in the marked stock. This was also true for the heterozygous deletion. The deletion which was confirmed cytologically consisted of either five or six bands missing from D7g or D8b in Griffen's map (Patterson, Stone and Griffen, 1940).

Apricot locus. Thirty-eight F_1 females had apricot eyes. These were grouped as seventeen deletions, eleven mutations, and ten undetermined. All of the new apricot mutations had the same appearance as the original mutation except one which appeared a little darker and slightly

more brown. It is distinguished with difficulty, however, as the original apricot darkens with age, and this must be taken into consideration. All cases which are lethal in the male also look the same as the original apricot when heterozygous with apricot.

The frequency with which the various loci were affected varies from 0.0667 for singed to 0.0154 for cross-veinless. White has the highest percent of viable mutations and also total fertility, and apricot the highest percent of deletions. Listed in descending order of percent they appear as follows:

Total cases	si	ap	w	v	dy	y	cv
Viable mutations	w	ap	si	y	v	dy	cv
Lethal or deletion	ap	si	cv	dy	w	v	y
Fertile cases	w	y	v	dy	cv	ap	si

NON-DISJUNCTION

While this experiment was not suitably set up for a critical study of non-disjunction, it seems justifiable to analyze the data and decide why the results given in table 3 do not correspond to other data published by various workers.

By employing the cross of untreated homozygous mutant females to treated wild type males two classes of non-disjunction could be recognized in the F_1 generation. These are wild type males containing their father's X, of which eight were found, and mutant females containing both their mother's X chromosomes, of which sixteen were found. Both of these classes are the results of non-disjunction in the untreated female parent. No means was readily available to distinguish XX from XXY female parents in the mutant stock used. Six of the wild type males found were sterile and assumed to be XO males resulting from primary non-disjunction. However, two of the wild type males did produce offspring and cytological examination of brain cells of their offspring revealed the normal complex of ten rods and two dots and the salivary chromosomes did not indicate a translocation. These two cases can be explained either as the result of contamination or, more probably, secondary non-disjunction.

Ten of the sixteen non-disjunction females produced offspring. Cytological examination of the brain cells in five of these cases was made; some of their female larvae offspring showed eleven rods and two dots indicating that they were XXY females. Primary and secondary non-disjunction females were not distinguishable. Two cases of secondary non-disjunction were obtained from approximately 400 F_2 flies when these females were mated to wild type males.

Using all twenty-four of the above cases, one male in 10,400 F_1 females was obtained and one female in 5,200. The sex ratio was two females to one male. Results obtained by Arai (1930), Demerec and Farrow (1930), and Kikkawa (1932 & 1937) in their untreated control series are summarized here for comparison. Only their counts of females are given.

	One Female in	One Male in	Female:Male
Arai	4600	2700	1:1.7
Demerec and Farrow	10,600	900	1:11
Kikkawa	8537	530	1:15
Girvin (treated males)	5200	10,400	2:1

The rate of one female in 5,200 is in closest agreement with the data obtained by Arai. This may be due to the

fact that he used a yellow stock as was used in this work. According to Kikkawa (1932), the presence of the yellow mutant increases the rate of primary non-disjunction.

HYPERPLOID MALES

One would expect when irradiating mature sperm that segments of the wild type X chromosome would be lost through breakage of the chromosomes. These deficient sperm would then produce either hypoploid females or hyperploid males depending upon the length of segment lost. Thirty-eight such individuals were found, or approximately one in 2200 of all F_1 X-bearing sperm that produced adults. Small deletions involving one locus or two loci in the case of cross-veinless and vermilion are not included in these data nor were the mosaics which will be treated in another section of this paper.

Thirty-seven of the thirty-eight hyperploid males were phenotypically ec cv v si dy ap. These probably resulted from deletions with one break between y and ec, and the second to the right of apricot (a region comprising perhaps one-third of the chromosome). The one exception was one individual showing + + cv v si dy ap. It differed only in that the segment of the wild type chromosome extended from between ec and cv to the left end.

All of the above flies were sterile as would be expected if they contained no Y chromosome. They were characteristictly smaller than their brothers and sisters

but they often lived for three to four weeks as adults. Except for their small size, they were well developed males with normal appearing genitalia, except for two individuals that had no external genetalia or anus opening. This condition occurred in the parent stocks and is not diagnostic. Thus, the segment between ec and cv to the left end, when duplicated in the male, does not seem sufficient to alter the external appearance of the male characteristics. It also seems that when the length of this segment is increased death to the individual results rather than a perceptable shift of male characters toward femaleness. This is comparable to the results found by Patterson, Stone and Bedichek (1937) for male X hyperploids in Drosophila melanogaster.

No hypoploid females were found which contained a large enough deletion for two of the marked loci to be affected except the cases involving cv and v which are only 0.5 cross-over units apart.

MOSAICS

Twenty-four F_1 female mosaics were produced showing the effects of a recessive mutant gene only in part of that body area where the effects would be expected to show. There were eight cases of yellow body color mosaics, seven cases of singed mosaics, eight individuals having one wing normal and one dusky, and one individual which was mosaic for dusky and singed. These are listed in table 4 with the types of offspring produced by each.

Mosaics may result from mutations or chromosomal rearrangements which occur in one of the chromosomes of the zygote after fertilization takes place. The extent of the body area affected and the genotype of offspring have been used as a basis for estimating in which division or stage of the embryo the change occurred. An alternate explanation of mosaic formation is that the chromosomes of mature sperm are sometimes in the two strand stage when irradiated so that only one of the strands is affected by the breaks or mutation. After fertilization the two genotypes from the paternal chromosome segregate producing a "half and half" mosaic. These two hypotheses were studied by Patterson (1933) and Moore (1934).

The mosaic individuals, all of which were females, were backcrossed to recessive males. A summary of these

crosses is given in table 4, and diagrams showing these mosaics are given in the appendix. All of the yellow mosaics produced numerous offspring as might be expected from those cases involving the yellow locus given in table 2. Case 1 was obviously a mutation because the yellow areas were not of the same appearance as y^{40a}. The bristles were dark and the body was more darkly pigmented. The female was almost a perfect example of bilateral symmetry except for its head which was normal. Apparently none of the chromosomes containing the new mutation got into the gonads as it did not appear in any of the offspring, which were equally divided as to males and females and y^{40a} and normal flies. Inbreeding of both classes failed to recover the "new" yellow.

Cases 2 and 3 were approximately half yellow and half normal but with very little summetry of the colored areas. Neither case produced any normal colored offspring. They apparently were the result of point mutations similar in appearance to y^{40a} because half of the offspring were y / and half were y ec and males and females were produced with equal frequencies. Examination of salivary gland chromosomes of both F_2 and F_3 females showed no abnormalities.

Slightly less than one-fourth of the body surface of

case 4 was yellow. It also appears to be due to a point mutation because of the yellow offspring which were twice as numerous as the normal; y males and females occurred with a little more than half the frequency of y ec flies. Crossing-over could account for only a small percent of the y individuals. Salivary gland chromosomes of F_3 females from all three classes of F_2 females appeared normal.

Cases 5, 6, 7, and 8 varied in the extent of yellow and normal areas of body surface and none show particularly regular patterns. Offspring from all four cases were approximately evenly divided between normal and yellow males and females. Of the yellow offspring only a few y individuals were produced which would be expected from crossing-over. Salivary gland chromosomes of F_1 females from 6 and 7 were normal; the other two cases were not examined. Therefore, it seems that the altered chromosomes of the F_1 were not recovered in the F_2 so there is no way to determine whether the mosaic formation was due to mutations, deletions, or other abnormalities. Later generations of both normal and yellow F_2 flies failed to give abnormal classes.

For the three cases in which the affected chromosome was recovered the evidence indicates a simple point mutation. The first case, in which the affected chromosome was not recovered, is considered to have been a point

mutation to an allel darker than y^{40a}. Thus, it seems likely that a majority of the last four undetermined cases were mutations likewise. This is in agreement with the thirteen yellow females in table 2 where eleven were viable point mutations and one was a lethal. It is also of interest that all eight of the yellow mosaics produced offspring and twelve of the thirteen yellow F_1 females were also fertile.

Somewhat the same correlation can be made with the singed mosaics and completely singed females, neither of which were particularly viable. Four of the eight singed mosaic females either produced no offspring or too few to be be analyzed. Twenty-seven of the fifty-six F_1 singed females, or about one half, are in the undetermined category. However, almost half of the singed females contained lethals whereas none of the three singed mosaics, from which the affected chromosome was recovered, contained a lethal.

Case 9 is interesting in that only about one-fourth of the body surface was covered with normal bristles. If one strand of a two strand sperm carried the singed mutation, or if the mutation occurred after the first nuclear division of the zygote, only half of the body area should be affected. The explanation probably is that there is no rigid predetermined fate for the nuclei resulting from

the first eight divisions. Flies that are "half and half" may be divided bilaterally or into anterior and posterior regions or into scattered areas. Thus, the proportion of a fly's body which is affected does not seem to depend upon the percent of the original 256 nuclei which contained the mutation, but rather the proportion of such nuclei that by chance get into cells which become the imaginal discs from which the exterior of the fly is formed. By the same reasoning mosaics with less than one-half of the body affected could still contain the mutated gene in one of the first two nuclei formed. Such cases need not be considered mutations in the soma. Whether the mutated chromosome gets into the germ cells and in what proportion is a matter of chance. According to Huettner (1923) and Rabinowitz (1941), varying numbers of the original 256 nuclei enter the outpocketings of the posterior region of the polynuclear embryo which later become the germ line. Rabinowitz found that of these not all were destined to become germ cells; of the thirty-six to seventy-three primordia initially present, only fifteen to forty-four are ultimately included in the amino-proctodeal invagination. From this invagination some of the germ cell primordia migrate through the gut wall before reaching the future gonad. Counts by Poulson (1937) and Sonnenblick (1941) on a large number of gonads reveal that the number

of germ primordia in each gonad varies from four to thirteen. Thus, eight to twenty-six cells from the once thirty-six to seventy-three have a chance of being transmitted to the next generation. When to this chance is added the fact that only about one hundred adults are obtained by ordinary culture methods out of the several thousand eggs which a female can lay, it is not at all surprising that the affected chromosome often is not recovered even though half the body is affected, or is recovered even though less than half is affected.

Case 9 and 11 produced no wild type offspring; these were about half males and half females, and almost half of these were of the ≠ si ≠ phenotype which indicates a point mutation. Case 10 can be declared a point mutation on the same basis. It also produced two males and three females which were completely normal. In all cases individuals of both F_2 phenotypes bred true in succeeding generations. Salivary examination of 9 and 11 revealed no abnormalities.

Case 12 produced one hundred and thirty-six wild type offspring and ninety singed offspring, of which three were ≠ si ≠ flies; these could be accounted for as double crossover cases. This case may represent a lethal or a deficiency.

Cases 13 and 15 produced only six and seven offspring

respectively and case 14 none. Case 16 was mosaic for singed and probably for dusky as one wing was normal and the other appeared dusky. No offspring were produced, but if both the loci were affected, it must have been due to a rearrangement affecting the singed dusky region and possibly apricot and the rest of the X to the centromere. The head was normal for singed so apricot eyes would not be expected to show.

Of the eight mosaic females with one wing dusky and one normal all produced offspring. Individual results are not included in table 4 for these mosaics because they are all similar and none indicate that the affected chromosome was recovered.

No mosaic was found for any of the other loci used in this work. However, three white mosaics were found in previous work using the same method, but different marked stock. One of these cases contained a translocation involving the X chromosome.

Patterson (1933) obtained one yellow mosaic from 1700 sperm calculated for 3000 r units for melanogaster whereas the eight yellow mosaics in virilis were produced at the rate of one in every 10,500 sperm treated with the same number of r units. He also lists twelve cases of yellow-gray male mosaics. One individual found in virilis which may be comparable to these is described in the list

of special cases, as it seemed to have been a hyperploid XO male which lost the paternal fragment carrying the normal allel for yellow after fertilization to produce a characteristic yellow mosaic.

GYNANDROMORPHS

A total of thirty gynandromorphs was found. As far as could be determined these were the results of a loss of the whole of the paternal wild type X chromosome. Thus, all areas of the fly's body which showed the recessive mutations of the maternal X chromosome are male tissue. No cases were determined to be gynandromorphs which showed loss of only part of the X chromosome. One case described as a mosaic for singed and dusky probably resulted from a break in the chromosome with later loss of one fragment. A second exception was the fourth individual described under special cases. In this case the echinus, singed, and apricot loci were involved. Diagrams of these exceptions and the gynandromorphs are given in the appendix.

No gynandromorph was found which could not be explained by a single loss of the paternal sex chromosome with the possible exception of two. Three-fourths of the body of these individuals were male tissue. This condition could have been the result of a single loss of the wild type X chromosome in the first division of the zygote with a distribution of cells to the imaginal discs which resulted in an unusually high proportion of male nuclei. Based on the method of the number of imaginal discs which form the various segments of the surface of the fly's

body, described by Patterson and Stone (1938), each had thirty of the forty discs containing male tissue plus the external male genitals. The mosaic number 9 is a similar case in which about three-fourths of the body is singed or twenty-seven of the forty imaginal discs have the altered chromosome. It is relatively simple to conceive of two succeeding mitotic divisions being abberrant, resulting in two losses of the X chromosome in order to produce a gynandromorph with three-fourths male tissue, but it is not as probable that two successive mutations occurred to produce the mosaic which seemed to be the result of mutation rather than a loss. Thus, it seems possible for the descendants of the first two nuclei to be present in the proportion of 3:1 in the body surface. The argument in favor of the double loss is that numerous half and half gynandromorphs were produced having twenty male and twenty female imaginal discs. Only one case exceeded this ratio and it contained twenty-two male discs.

Eleven of the remaining twenty-eight cases were almost one-half male and one-half female, except for the one mentioned above which was slightly more male than female. Even though virilis contains one extra segment which is fused to the seventh in melanogaster, it is so small no record was made of its mutant characters, and the tissue derived from forty discs is considered the

total. All of these cases were primarily bilaterally divided, that is approximately one-half of each major portion of the body was male and the other half female, regardless of whether male parts were on the right side in one part and on the left side in another part or all on the same side. Of the eleven, however, four had all male heads and two had all female heads. Corresponding tissue was compensated in the abdomen so that they still contained only one-half of each type of tissue.

In contrast to those which were basicly bilateral there were none which were divided into anterior-posterior regions; that is, with head and thorax one sex and abdomen the opposite sex.

There were seventeen cases which contained approximately one-fourth or less male tissue. These varied considerably in extent, from three cases where there was only a yellow, singed spot on the thorax, to cases which were male in almost one-third of the body. In six of these cases the male tissue was almost entirely limited to the head, and in three cases to the thorax. These three represent the smallest areas of male tissue of all the gynandromorphs. One individual contained male tissue in the thorax and abdomen only and although this included about one-fourth of the external body area all of the male tissue was on the dorsal surface. Six individuals had patches

of male tissue on the head, thorax, and abdomen. Only one case was found which was considered to have the male tissue limited to the abdomen and in this case one posterior leg was also male. Thus, the head was most often affected, the thorax second, and the abdomen least. In the majority of these cases the dorsal surface was more widely covered with male tissue than the ventral surface. This is partly due to superficial causes due to the shape of the fly and in part due to actual number of segments affected. The ventral surface of the thorax being a lighter color would make detection of small, yellow mutant areas more difficult than if it had occurred on the dorsal surface. This coupled with the fact that the wings hid the dorsal surface of the abdomen may, in part but probably not entirely, explain the greater frequency of cases having the head affected over those which had the abdomen affected.

The areas of male and female tissues in virilis are more irregularly distributed over the body and do not seem to follow segment boundaries as sharply as in cases described for melanogaster by Patterson and Stone (1938). A possible explanation of this may be the manner in which the nuclei are distributed to the ectoderm from which the imaginal discs are formed by invagination. Many important details of the imaginal disc formation are as yet unknown

(Poulson 1937). It is known that they are formed by invagination of the ectoderm at various points on the periphery of the 18-22 hour embryo. The regularity of the exoskeleton pattern derived from these discs would depend on several variable factors which as yet are undetermined. These variables are: (1) the mosaic pattern of male and female tissue of the ectoderm. If the number of mitotic divisions resulting in the formation of the ectoderm is relatively large, the size of male and female areas would presumably be correspondingly large, with an increased possibility that all of the cells of a particular invagination would be of the same sex. If the number of mitotic divisions is relatively few, a mosaic pattern of the two types of cells would be correspondingly small and the probability of a particular invagination containing both types of cells is increased proportionally. (2) The size of the invagination as measured by the actual number of cells which go into the formation of the imaginal discs has the same relative value as the size of the areas of male and female tissues of the ectoderm. Thus, the difference in the regularity of the pattern of the adult exoskeleton of virilis and melanogaster may be in the manner of imaginal disc formation.

A second explanation of the difference may be that the early cleavage divisions of melanogaster are more

nearly determinant than they are in virilis, and thus the distribution of male and female nuclei to the region from which the ectoderm will be formed is more regular.

SPECIAL CASES

A few individuals found during the course of this work did not fit into any of the classes already described. These are grouped together here under the heading of special cases.

1. A male was found which showed the phenotypical effect of all of the recessive mutations except that one wing was normal instead of dusky. The simplest explanation of this male is that a somatic, reverse mutation occurred spontaneously in the untreated X chromosome sometime after fertilization so that only one wing was affected. Although the fly lived about two weeks no offspring were produced.

2. One F_1 female showing ≠ (ec?) (cv?) (v?) si dy ap was produced. It is possible that the only mutant genes were si, dy, and ap because the body color was completely normal. Both eyes, though resembling echinus, may merely have been rough and both wings had partial cross-veins and thus, may not have been cross-veinless. Vermilion cannot be determined when apricot is homozygous. All the head and thorax bristles were singed, but the abdomen hairs were not. Both eyes were apricot and both wings dusky. The phenotype of this female was probably the result of a loss of the right section of X chromosome in

the head and thorax region. If this is true, the abdomen should contain two complete X chromosomes and produce typical female genitalia. The length of the segment lost cannot be determined except to say the break occurred somewhere between singed and yellow.

3. One male showed all of the mutant characters and in addition showed extensive patches of normal body color on the thorax, abdomen, and both wings. One wing contained a cross-vein which was surrounded by normal tissue; the other wing was yellow in the same area, and no cross-vein was present. The dark patches on the thorax and abdomen contained singed bristles and hairs. This individual probably originated as an egg containing an X chromosome with the mutant genes which were fertilized by a sperm bearing only the fragment of the treated wild type X containing the normal allels of yellow, echinus, and cross-veinless. Thus, the customary hyperploid male containing a longer fragment than any obtained in this work would have resulted except for subsequent loss of the fragment in one of the early nuclear divisions. All of the head was yellow and both eyes were echinus because the fragment was not present in the head cells. In addition both of the posterior legs had elongated tibia which were curved almost into a semicircle. This male was sterile, presumably because it contained no Y chromosome.

4. A fly possessing typical male genitalia had completely normal body color, wings, and cross-veins. About two-thirds of one eye was apricot and echinus, the remaining third, and all of the other eye being normal. There were six singed bristles which were scattered over the thorax and head. Two of the singed bristles were almost in the center of the dorsal side of the head, one on the humeral hump, one on the scutellum, and three on the ventral and lateral portion of the mesothorax. Possibly by coincidence, the six singed bristles and the mutant part of the eye were all on the right half of the body.

The best explanation that can be offered for this case is that the X chromosome was broken between yellow and echinus, and the right hand portion was lost late in development in such a way that the portions of the head, thorax, and the genitalia were affected.

YELLOW MOTTLE

One yellow mottled F_1 female was found. Cytological examination and genetic tests of her progeny proved that it involved a mutual X-6 translocation with the break in the X chromosome immediately to the right of the yellow locus. The original mottled female was backcrossed to the mutant stock and proved to be quite fertile. The F_2 generation showed apparently normal crossing-over throughout the entire length of the X chromosome with one-half the females showing yellow and one half mottled. However, there were more than twice as many females as males. Mottled females which have just come out of their pupa cases are practically identical in appearance to yellow females except their wings and some bristles are slightly darker. Within ten to thirty minutes, however, the whole body of the fly is speckled with dark spots. The appearance of adults from twelve to seventy-two hours old is the normal dark body color of virilis with yellow patches covering the entire body, but most easily observed on the abdomen and sides of the thorax. Some flies have smaller spots and are generally darker than others. As the flies age the yellow areas disappear so that after about a week the body color appears completely normal. When the flies are heterozygous for y^{40a} some of the bristles and hairs

including the pile on the ommatidia are also yellow as they are in homozygous yellow flies. These differ from the body color in that they do not darken with age so that an old, mottled fly appears normal with a yellowish hue super-imposed by part of the hairs. The wings also have a yellow glint, particularly in the anterior portion. When females are heterozygous for y^1, an allel of y^{40a} that is not as bright a yellow and does not cause yellow bristles, mottled flies can be distinguished from their y^1 brothers and sisters with difficulty when young and only rarely when old.

In the third generation two mottled females produced three mottled males; two of these were fertile both with mottled females and yellow females. Mottled males, generally, have the same appearance as females except they usually are smaller and weaker and frequently are sterile.

The cytological examination of the salivary chromosome revealed the X to be broken at A3b or c (Griffen's map in Patterson, Stone and Griffen 1940) and replaced by almost all of the sixth chromosome broken at about A3g. The ordinary preparation showed the left end of the X free of the chromocenter with the translocated piece of the sixth and the haploid portion of the X branching from the end. At the chromocenter the rest of the sixth and the tip of the X could be seen but it was not definitely

identified as such. In order to determine whether the yellow locus was in this translocated fragment, mottled females heterozygous for y^{40a} were mated in pairs to se y^{1} sc males. Sepia is located at 0.1, y^{1} at 2.9, and scute at 3.8 on the linkage map. Fig. 2 illustrates this cross by diagrams of the X and sixth chromosomes on which the loci in question are located. There are eight possible types of female gametes (including non-disjunction types) shown in the left column. The classes of offspring which each of these produces in combination with the X and Y sperm are shown in the squares containing the classes A through P. The phenotype of each individual is given in the lower part of each square. The terms hypoploid and hyperploid refer only to the X chromosome.

Some of the classes appear very infrequently or not at all in some cultures. A typical count of the phenotypes was obtained from the first five paired matings made and are given below.

A and C. 125 Mot/y^{1} female (2 classes)

B. 49 se y^{1} female (hypoploid)

D. 85 y^{1}/y^{40a} females

G. 12 se y^{1} sc males

H. 4 Mot/y^{1} sc males

I and K 4 Mot/y^{40a} males

L. 102 y^{40a} males

M. 3 y^{40a}/y^{40a} females

These classes can be accounted for if the translocated fragment of the X contains the normal allels of sepia and the y^{Mot} loci and can segregate independently of the other portion which contains the scute locus and all the genes to the right. This is illustrated in Fig. 2.

The two classes A. and C. are of the same appearance but are derived from two different types of eggs. The difference in genotypes can be demonstrated by mating a large number of these Mot/y^1 females individually to se y^1 sc males. Based on the phenotypic class represented in the offspring the parents can be distinguished as either Mot/y^{40a}/y^1 females (triploid for the left tip of the X representing class C.) or Mot/y^1 females representing class A. Fig. 3 shows diagrams of these crosses with the phenotypes obtained. There are three classes which do not appear in both crosses which are used to distinguish the genotype of their mothers. These three classes are bracketted in heavy lines and are as follows:

From Class A. Female	From Class C. Female
se y^1 female	y^{40}/y^1 female
	y^{40} male

Class B. females were derived from type 2 eggs and are hypoploid for the se y^1 region. They were small, weak, and seldom produced offspring. They frequently had

doubling of one or more of the scutellar bristles which were often longer and more slender than normal. Other classes of flies gave this same effect. This appearance is thought to be caused by the effect of the proximity of the break on the scute locus. It also occurs in cases where the mutant scute gene is not involved, and will be discussed later.

The offspring of this class, when crossed to y^{40a} males, produced, as expected, se y^{1} sc males, y^{1}/y^{40} females, and y^{40a} females which were hypoploid for the left end of the X like their mother. The corresponding hypoploid male dies so twice as many females as males are expected, which is what is actually found. The y^{1}/y^{40} females when mated to se y^{1} sc males can be shown to be heterozygous for se and sc.

Class D. females, y^{1}/y^{40}, are the result of an X bearing sperm fertilizing an egg of type 4.

Classes G. and H. which are the result of non-disjunction carry their father's X chromosome and a sixth chromosome from their mother. Class H. actually gets very little of its mothers sixth which has been replaced by the fragment of the X chromosome. These classes appear with a surprisingly high frequency as indicated by the sample count above. They are always sterile.

Class I. and K. males, Mot/y^{40a}, appear frequently

in some cultures and rarely or not at all in others. Some females give about equal numbers of mottled and yellow males. Nevertheless, they represent individuals from two types of eggs, 1 and 3, which cannot be distinguished by observation. Both are usually smaller than the normal male and slightly darker than their mottled sisters.

When mottled males of classes I. and K. are mated individually to se y^1 females their origin can be determined by the classes of offspring produced. Fig. 4 shows these classes with the two distinguishing classes bracketed in heavy lines. They are:

Class I. Males	Class K. Males
se y^1 female	y^1/y^{40} female

Class L. males, y^{40a}, are by far the most numerous and are the result of type 4 eggs being fertilized by a Y bearing sperm.

Class M. and N. are the result of non-disjunction and occur relatively infrequently. Class M., y^{40} female, occurs about once in every two hundred offspring and Class N. slightly less frequently. Both classes are fertile. The only difference between the two is that N. is hyperploid for the tip of the X which replaces part of the sixth chromosome and therefore is mottled; whereas, M. is normal except for the Y chromosome and is phenotypically yellow.

Thus, it can be shown that the break in the X chromosome is between y and sc so that se and y segregate independently of sc which is to the right of the break. It is also seen that the fragment contains the normal allel for se and the mottled "normal" allel for yellow.

In order to follow the translocated fragment in relation to the sixth chromosome and also to test its linkage to mottled, Mot/y^{40a} females were mated to y^{40a}/ac gl males. The reciprocal cross was also made but due to the small amount of crossing-over in the se y sc region and in the short sixth chromosome the results were the same. Four classes were obtained; y/≠ ≠ and Mot/≠ ≠ females and males. Very few of the mottled males were produced. The above classes are not accurate in that some of the mottled flies were acute but not glossy. They are not listed as acute since this character is very difficult to distinguish, due to overlaping with normal. However, a few were definitely acute. Thus, the break in the sixth is between ac and gl so that when a type 1 or 3 gamete (Fig. 2) is involved, an individual haploid for most of the sixth (but not gl) results. The question of whether triplo-six individuals are produced is more difficult. They would result from type 2 gametes with an egg or sperm containing a normal X and sixth. It was not possible to demonstrate this class genetically due to the low viability

of females hypoploid for part of the X and the inconclusive nature of acute. However, cytological examinations revealed the translocated part of the sixth attached to the tip of the X in daughter larvae from non-mottled parents, indicating that they do occur.

A few cases haploid for gl were obtained. From about 1200 offspring from Mot/y^{40a} females X y^{40a}/ac gl males six yellow females with glossy eyes occurred which apparently were not acute. They must have originated as type 1 eggs with the translocated fragment causing mottling and the maternal fragment of the sixth containing the normal allel for glossy being lost in the early zygote so the then haploid glossy was apparent. A seventh case was a Mot/y^{40a} female which was of customary appearance except one eye was glossy and the half of her head containing the glossy eye was y^{40a}. This seems to have been a case similar to the other six except the loss occurred later in development. When mated to y^{40}/ac gl males one of the y^{40a}/gl females produced a few y/gl offspring; the Mot/y^{40a} female with one gl eye produced classes of offspring which were both mottled and non-mottled and with gl and normal eyes.

Cytological examinations of larvae salivary glands were made in an effort to correlate cytological evidence with that which was obtained by breeding tests. A group

of mottled females from a stock which had been maintained from the original female by matings to y^{40a} males were individually mated to se y^{1} sc males. These were transferred to new vials every two days to obtain good larvae for cytological work, but all the vials containing eggs laid by a single female were kept grouped together. When larvae were available the slides were made and examined. If the translocation was found, that is if the left end of the salivary X chromosome contained one normal X and one bearing the translocated piece of the sixth, the vials were marked and the remaining larvae allowed to develop. If the translocation was not found in five to eight larvae, the vials were labeled as containing "normal X chromosomes", and also allowed to continue development. From those vials which contained the translocation all possible classes appeared as given on Fig. 1. Thus, the original female was of Class A. From those vials which did not contain the translocation only two types of females were obtained, y^{1}/y^{40} and y^{1}/y^{40}/Mot. Thus, the original female was triploid for the left tip of the X chromosome and all of her mottled daughters were also; whereas, those parents that contained the translocation produced some mottled daughters like themselves and some which were not.

The term "translocation" in the foregoing paragraph

indicates only that part of the X chromosome which was replaced by the fragment from the sixth. It is not intended to indicate the condition of the chromatin which segregated with the sixth centromere. The tested females were mottled and necessarily had the fragment of the left end. Due to the small size of the translocated segment of the X, it was not possible to visibly identify it as such; however, because of the lack of synapsis of non-homologous parts, the "sixth" chromosome appears distorted with bands sometimes lying at right angles to one another.

The presence of the fragment of the sixth chromosome on the tip of the X can be found among the offspring of non-mottled flies but usually not with a very high frequency. These are the females which develop from type 2 eggs and are deficient for part of one X chromosome.

Salivary gland chromosomes of male larvae did not supply any conclusive evidence. As mottled males occur rather infrequently, there is no certain way of knowing when a mottled has been included in the number observed. Of all the larvae observed only one may not have been normal. In this case the X chromosome appeared normal, but at the point of breakage the sixth chromosome appeared to be attached. While this is a doubtful case it may have represented a male from a type 1 egg that has only one

tip of the X chromosome which is attached to the sixth. If this were the case, then the two sixth chromosomes were synapsed carrying the tip of the X along with them making the X appear normal.

While mottled males have not definitely been examined cytologically, the following procedure was used to establish their chromosome arrangement. Mottled males were individually mated to y^{40a} females from the regular stock and the salivary glands of their daughter's larvae examined. Part of the daughters of some males showed the translocated sixth chromosome fragment attached to the left end of the X while none of the daughters of other mottled males were found showing any evidence of the translocation. This is in agreement with the evidence obtained from breeding tests that two types of mottled males are produced (Fig. 4). The one whose daughters do not contain the translocated sixth fragment are hyperploid for part of the X.

All metaphase plates made from larvae brain tissue appeared normal. The two dot chromosomes were always of the same size. This is not particularly surprising as the salivary size of the two fragments exchanged are approximately equal.

The mottled effect seems to be produced by a delaying action on the production of dark melanin pigment in some

areas of the fly's body and almost normal production of the pigment in other areas. Flies homozygous for the normal allel of yellow are very light when they first emerge from their pupa cases and darken with age. The mottled flies differ only in that some parts darken more slowly than others and even the darker portions are about twenty-four hours behind the normal fly. The bristles and wings normally are already pigmented when the adult emerges. This is true also for mottled flies except that some bristles contain dark pigment and some are yellow. The bristles of mottled flies do not undergo the same darkening as the rest of the body; it therefore seems that the cause of the mottling is effective in the late pupa stages and the first few days of the adult stage. The dark melanin pigment is known to be a non-diffusable substance from cases of mosaics and gynandromorphs. In these cases yellow parts of the body do not contain the normal allel for yellow. In the case of mottled flies, on the other hand, all cells presumably do contain the normal allel. This normal allel seems not to function with normal efficiency in its new position near the centromere of the sixth chromosome in any of the cells and less so in some areas than others.

In considering the order of dominance of mottled flies in the yellow series the age of the individual must

be considered. Mottling appears the same as the normal allel in old flies when body color alone is considered. In young flies mottling is dominant but the characteristics of the particular yellow allel can be distinguished. Thus, Mot/y^{40} appears almost as yellow as y^{40}/y^{40} flies but has some dark hairs and bristles, the wings are darker, and the body is covered with small dark spots which will eventually turn the whole body normal color. Mot/y^{1} flies are about the same in appearance as y^{1}/y^{1} flies except for the dark spots on the body. No bristles are yellow which is characteristic of y^{1}. Thus, as the individual darkens it takes on a completely normal appearance. Mot/normal appears completely normal throughout.

Often mottled males seem to be a little darker than their sisters. This might be due to the presence of extra heterochromatic Y chromosomes in XYY males as non-disjunction occurs frequently. Cases where the presence of an extra Y chromosome tended to lessen the variegated mutant effect, thus, producing a more normal individual, have been reported by Gowen and Gay (1933), Stone (1937). However, the presence of a Y chromosome in the female does not seem to suppress the mottling expression. Mot/y^{40} females were mated to normal males bearing the dominant X chromosome mutation, Beadex. From approximately 800 to 1000 offspring three y^{40} females and four Mot/y^{40}

females were found. The Mot/y^{40} females were of the customary mottled appearance, seemingly unaffected by the presence of the extra Y chromosome. One was mated again to the normal Beadex males and produced one female like herself, but no mottled males. The other mottled females were mated to y^{40} males. All of the mottled daughters were of the usual variegation. Again no mottled males were produced. None of the non-disjunction yellow females produced offspring, thus, it seems that the presence of a Y chromosome in a female does not affect mottling. No XYY males have been recognized, but they may be the darker males that are occasionally found. Slides were made of the brain tissue of daughter larvae from all of the non-disjunction mottled females to make certain they contained the extra Y chromosome. About one half of all slides in each case showed eleven rods and two dots indicating the Y was present.

The variable number of scutellar bristles was mentioned above. This variability is quite sporadic and probably should be considered as a mottling effect. When mottled females are mated to yellow males about 10 percent of the yellow daughters have five to eight scutellar bristles and about 5 percent of the mottled females show the same increase in some of the cultures. The yellow

females not only show an increase in bristles, but are small and often are sterile. Cytological studies of their daughters show they contain the broken X chromosome. Genetic tests show that those females hypoploid for the se y region are the ones which have the increase in bristle number. Thus, flies which contain an X chromosome broken just to the left of the scute locus often, but not always, show doubling of one or more of their scutellar bristles. This doubling occurs about twice as frequently in yellow flies as in mottled ones indicating that when the translocated genes, which normally lie to the left of the scute locus, are present in the cell, even though they are not attached in the customary manner, the flies are more often normal.

Flies which are hyperploid for the left end of the X often show a reduction in the number of scutellar bristles. These are only the mottled males and females because the yellow flies are never hyperploid. The frequency that flies are found which show this reduction varies from culture to culture. In some up to 30 percent are affected but in others as low as 1 or 2 percent show the reduction. Flies of this class usually have two or three scutellar bristles but some have only one or none at all. There is no appreciable difference in the number of males and females. There seems to be a balance between

the normal allel of scute and some gene or genes to the left of the scute locus for the production of the scutellar bristles.

It has not been possible, as yet, to obtain a homozygous stock for mottling though theoretically this should be possible by mating non-hyperploid mottled females to non-hyperploid mottled males.

LIST OF MUTATIONS

Most of the mutations at the marked loci have the same appearance of those originally used and will not be discussed. There are five which differed in phenotypic expression which will be described below. No dominant mutation was found which would live homozygous except three which were associated with translocations. Those mutations which would not live when homozygous are not listed.

1. $\underline{y}^{47i}$. This is an allel of $\underline{y}^{40d}$ and was found several times. It gives a brighter, more orange color to the eye than $\underline{y}^{40d}$. When homozygous with apricot the eye pigmentation is reduced. An almost white eye is obtained by $\underline{y}^{47i}$ $\underline{w}^{e}$ $\underline{ap}^{40}$ whereas, $\underline{y}^{40d}$ has no interaction with apricot or eosin apricot. $\underline{y}^{40d}/\underline{y}^{47i}$ is slightly different from homozygous $\underline{y}^{40d}$.

2. $\underline{y}^{47j}$ is an allel of y about the coloration as $\underline{y}^{1}$. It gives the same expression homozygous, hemizygous, or with $\underline{y}^{40a}$.

3. $\underline{y}^{48a}$. This is an allel of $\underline{y}^{40a}$ which is almost normal. The normal pigmentation is diluted giving a pale body color. The same expression is obtained from $\underline{y}^{48a}/\underline{y}^{48a}$, $\underline{y}^{48a}/\underline{y}^{40a}$, or when hemizygous.

4. $\underline{y}^{48b}$. This is also an allel of $\underline{y}^{40a}$. The body color

is slightly yellow. Yellow is more pronounced on the wings. The same expression is obtained from $\underline{y}^{48b}/\underline{y}^{48b}$, $\underline{y}^{48b}/\underline{y}^{40a}$, or when hemizygous.

5. $\underline{ap}^{48a}$. This is an allel of $\underline{ap}^{40e}$ but is a little darker and more brown when homozygous or hemizygous.

6. A dominant wing mutation associated with a 2-3-5 translocation. The wings are slightly shortened, often cupped, spread 30 to 45 degrees, and less transparent than normal. LII is missing or rudimentary. The anterior cross-vein is partially missing. LV is completely or nearly absent between base and posterior cross-vein. 3D posterior cell often broader than normal. Flies are weak and fertility is reduced.

7. A dominant eye mutation associated with a 2-4 translocation. The eye is eliptocal. The vertical axis is about twice as long as the horizontal axis. Fertility is good when heterozygous but reduced when homozygous.

8. A dominant wing mutation associated with a 2-4-5 translocation. The wings are extended 60 to 70 degrees, shortened and often notched. The abdomen is reduced in size. Fertility is very poor.

DISCUSSION

The normal allel at each locus seems to possess individual characteristics of mutability and also viability after mutation. There was no particular correlation between the mutation rate and the rate of deletion or lethal mutation at a particular locus. If we disregard the undetermined cases, the normal allels of y, v, dv, and w produced viable mutations more frequently than lethals or deletions. The normal allels of cv, si, and ap gave more deletions or lethals than viable mutations. Had the undetermined cases been considered as lethal deletions this relationship would not be altered for y, w, si, and ap. As white and probably y^{40a} are amorphs it may be that the mutant gene and a single gene deletion would give the same effect both in the heterozygous and hemizygous conditions. This has been demonstrated for y in melanogaster by Stern (1935) and Muller (1935).

Patterson (1932) has published data for fourteen loci in D. melanogaster similar to those obtained here for D. virilis. His method was comparable to that used here in that he mated treated males to marked females. Table 5 has been compiled from his table I and table 2 of this work. Six genes which are homologous in the two species are compared. Homologies are accepted on the bases of

the work of Sturtevant and Novistki (1941) and Chino (1937). The table is so constructed that comparison of the two species can be made, reading vertically and comparing the ratio of the three classes for a given locus in one species to that of the other species. The numbers themselves are not comparable as Patterson did not give the total number of flies observed nor did he use the same X-ray dosage. Also the number of cases for the different loci of melanogaster cannot be compared for actual mutation rates because they resulted from several different stocks used in different experiments. Finally, Patterson's figures for yellow may not represent all the cases, as yellow lies close to the viability gene located in the left end of the melanogaster X chromosome (Patterson 1932). If a break including both this viability gene and yellow occurred it would not be viable even in the female. Theoretically such a break should be included in the lethal cases. The cases for melanogaster which included both white and notched are deficiencies for this region and are thus included in the table and should be added to those for white when comparing with virilis.

Table 5 shows clearly that in every case for melanogaster lethals are produced for a particular gene more frequently than viable mutations, with the possible exception of garnet which gave four lethals to three viable.

This is not true in virilis for three of the six genes when the undetermined individuals are not considered. When the totals are considered for the six homologous genes, there are seven times as many lethals as viables for melanogaster, whereas, in virilis there are almost one-fourth more viables than lethals. The percent of undetermined cases of the total number of individuals is approximately the same for both species. The same general statements are true also when all fourteen genes for which Patterson gives data are compared with all eight for virilis.

Also of interest is a comparison of the number of mottles which were produced. Thrity-two white mottles were found in melanogaster which is one-half as many individuals as all the other cases of white eyed individuals combined while none were found in virilis. Only eight cases of white were obtained in virilis which is too small a number to reason that four mottles should be found. However, previous work done by the author and other persons (unpublished) using the same method failed to produce a single white mottle in 30,000 to 50,000 flies. Virilis did produce one yellow mottle while none was listed for melanogaster in Patterson's paper. However, body color mottles have been found in melanogaster (Stone 1938).

Demerec (1935) has published similar results obtained from two years work on different problems with melanogaster. Comparable data from his table I have been incorporated into table 6 for comparison with data from table 2 for virilis. The same restrictions must be observed for tables 5 and 6. That is, comparisons can be made only of the ratios of the numbers in the vertical columns. An additional fact must be kept in mind, that is, Demerec gave data only for loci which were most fertile.

Of the three homologous loci of white, dusky, garnet-apricot, the lethal rate was higher than the viable mutation in melanogaster, but not in virilis. There is a ratio of three lethals to one viable for melanogaster. For virilis the ratio is one to one. However, when the undetermined cases are all considered as lethals the melanogaster ratio remains 3:1 while the virilis ratio is 1.7:1. When all five genes are considered for melanogaster the ratio of lethals to viables is 2.3:1 compared to 0.8:1 for virilis when the undetermined cases are not included. If we consider all of the undetermined cases as lethals the ratio is 2.4:1 for melanogaster and 1.8:1 for virilis.

Thus, by comparing the results for virilis to the data given by both Demerec and Patterson for melanogaster, it is obvious that the proportion of lethals to viable

mutations is greater in melanogaster than in virilis, both for homologous loci and also for all loci for which information is available. The ratio of 2.4:1 obtained by including all undetermined cases as lethals in Demerec's data most nearly corresponds to the similar 1.8:1 for virilis. However, Demerec gave data only for the most fertile loci so that the proportion of lethals he actually obtained is probably higher than is apparent from his data.

It is very difficult to make direct comparisons of the mutation rates for a particular gene in two different species owing to various methods and dosage used by different authors. Usually only lethal rates of a whole chromosome have been studied owing to the obvious advantages of such methods over visible mutations. An effort will be made here to compare fragmentary evidence from numerous heterogenious experiments on melanogaster to the rates obtained in virilis. All of the calculations will not be given in the cases of more doubtful value.

Patterson (1932) treated gray scute^{8} apricot males and mated them to yellow scute miniature garnet forked females. The inversion associated with scute^{8} may have effected the results and thus make the following comparison with virilis unreliable. No mention was made of the dosage used. From the 4,800 F_1 females examined he found twenty-two yellow females, a frequency of 1/216 treated

sperm affected at the yellow locus. Assuming his t 14 dosage was used (the highest dosage mentioned during the series of problems he was working on at the time) the frequency when converted to 3000 r units would be approximately 1/255 treated sperm, a frequency far higher than any gene in virilis gave. Of these twenty-two F_1 females nine were sterile and thirteen were viable only in heterozygous females.

In a paper by Patterson and Muller (1930) in which they reviewed much of their previous work, a total of thirteen white mutations at the rate of 1/1800 treated sperm was obtained. When these results from several dosages were calculated for the t 12 dosage a frequency of 1/1000 (their figure) was obtained. In their count of thirteen white mutations four cases of fractionals with a value of 1/2 were included. If we subtract these cases, eleven mutations are left which occurred at a frequency of 1/1181 treated sperm at the t 12 dosage(approximately 3000 r units). The frequency for white in virilis was obtained as 1/2900 sperm treated with 3000 r units or less than one half (1/2.2) the frequency as found in melanogaster. These are rates at which viable mutations occur.

A comparison of the combined rate of viable and lethal mutations can be obtained from the results given by

Patterson (1933). He was studying the effects of X-rays on different ages of sperm in mosaic formation in melanogaster. The comparison is based on data taken from his table V using only the classes of flies which are comparable to virilis and only those results which were obtained for the first four days of mating so that the conditions of the two experiments would be similar. He obtained thirty-nine individuals which had the white locus affected from 19,182 females carrying the treated X chromosome. This amounts to one affected sperm in 500 for 3975 r units. Assuming these are all mutations or minute breaks so that they are produced proportionally to the dosage, a rate of one sperm in 700 was affected at the white locus at 3000 r units. Virilis produced only 1/2600 sperm at 3000 r units. Thus, melanogaster produced about twice as many viable mutations at the white locus as virilis and about four times as many viables and lethals combined.

If the proportion of lethal to viable mutations from the fertile cases in table 5 is used, 3.8 of the thirty-nine white-eyed females were viable mutations or occurred at a frequency of 1/6730 sperm treated with 3000 r units. If we use the ratio of lethal to viable mutations obtained by Demerec in table 6, five of the thirty-nine cases were

viable and would have occurred at a rate of 1/1031 sperm treated at 3000 r units.

Timofeeff-Ressovsky (1932) studied the mutation of the normal allel to white in an American and Russian strain of melanogaster. Using a dosage of 4800 r units he obtained one white allel mutation in 1148 treated sperm for the American strain and one in 1892 for the Russian strain. When converted to the equivalent of 3000 r units the rates are 1/1837 for the American stock and 1/3027 for the Russian stock. These were viable mutations which lived in the males.

Patterson (1933) listed seventy-six yellow females for the first four days of mating. These include all classes of lethal and vialbe mutations and those which were sterile. Thus, the yellow locus of melanogaster was altered once in 256 sperm irradiated with 3975 r units, or assuming that all cases were due to single breaks or mutations, once in 336 sperm when computed at 3000 r units. The yellow locus of virilis produced only one affected sperm in 6450 treated with 3000 r units. If we consider the fertile cases in table 5, there is a ratio of eight lethals to one viable at the yellow locus for melanogaster, which means only one-eighth of the F_1 yellow females were due to a viable mutation with a frequency of 1/2940 sperm

treated with 3000 r units. If all of the undetermined cases are considered as lethals then the calculated rate would be one viable mutation in 4797 treated sperm. Virilis gave one viable mutation in 7627 sperm given the same dosage. Thus, the yellow viable mutation rate in melanogaster is between 2.6 and 1.6 times as high as it is in virilis.

The above calculations are condensed into a table and the rates converted into percent. 3000 r units is used as the common dosage for comparison and all effects are considered to increase proportionally to the dosage.

	Yellow lethal and viable	Yellow viable	White lethal and viable	White viable
Melanogaster				
Patterson (1932)	0.39			
Patterson and Muller (1930)				0.09
Patterson (1933)	0.30	0.034 0.021	0.14	0.015 0.097
Timofeeff Amer. Russian (1932)				0.054 0.033
Virilis	0.015	0.013	0.038	0.034

All values for virilis are lower than those for

melanogaster except for one method of calculation for viable white mutations and that for the Russian stock. Thus, melanogaster gives not over twice as many viable mutations, at least for the yellow and white locus as virilis does, but is considerably more susceptable to X-ray treatment in the production of lethals, not only in these two loci but in all loci given in tables 5 and 6.

The rate of recessive lethal production in the X chromosome of melanogaster has been studied by various people with somewhat different results. Schultz (1936) summarized works of a number of geneticists on lethal production in melanogaster. Among those who used about 3000 r units were Schectmann with a rate of 5.98 percent at 2,260 r units and Timofeeff-Ressovsky at 7.5 percent at 2,400 r units. Demerec (1930) found twice the mutation frequency of sex linked recessive lethals in the Swedish-b stock of melanogaster as in the Oregon-R stock of the same species. All of these gave a considerably higher rate of lethal mutations than was obtained by Clayton (1946) for virilis, who used 4,650 r units to obtain 3.28 percent. However, Handler (1946), whose work paralleled that of Clayton, did not obtain a rate significantly higher for melanogaster. The low rates obtained by Clayton and Handler may be due to their not using the

CLB method frequently employed by the other authors. In view of the majority of the above work and the higher proportion of visible mutations which are lethal in melanogaster than virilis, it seems probable that the total production of lethals in virilis is less than in melanogaster.

Demerec (1935) stated the conclusion that the majority of recessive lethals are minute deficiencies from one to eight salivary chromosome bands in length. In the majority of the cases of visible mutations in melanogaster which were lethal hemizygous he was able to detect a deficiency in the salivary chromosome.

If most of the other loci of the X chromosome give the same proportion of lethal to viable mutations as was obtained in all the loci given in tables 5 and 6, the higher lethal rate found in melanogaster than in virilis can be explained by a higher susceptability of the melanogaster X chromosome to produce small deletions under the influence of X-ray treatment. The viable mutation rates for the two species are close to the same value indicating that the major difference is not in the mutability of the genes themselves, but in the resistance of the virilis chromosome to breakage.

An important point, so far ignored, is the manner in which deletions and mutations are produced. Mutations

of the viable type increase proportionally with the dosage as do lethal mutations. If deletions are to account for the lethal mutations found, they also must be produced proportionally. Evidence that minute deficiencies are so produced was found by Muller, Makki, and Sidky (1938). Probably deletions resulting from two breaks accounted for some of the visible, lethal mutations used in the calculations above, but no means is available for determining what proportion of the total number were thus produced. Probably the number is small enough so as not to affect the results. None of the cases checked, except the white deficiency, showed any visible changes, but it was not practicable to check all cases band for band.

The explanation that the virilis chromosome is more resistant to production of minute deficiencies than the melanogaster chromosome may not be accurate. It may be that they are produced as often but do not survive heterozygous in the F_1 female. This would give the same results as though they were produced less frequently as assumed above. A third explanation is possible. If the deletions involved only had one band they could be the result of a "mutation"causing an amorph in respect to autocatylitic activity. In this case virilis mutated to this "amorphic allel"less frequently than does melanogaster.

Regardless of which of the three possible explanations of how the experimental results are produced, when the actual number of flies that survive is considered there is a significant difference in melanogaster and virilis. The proportion of lethal mutations found in melanogaster is from three to seven times the number of viable mutations, whereas, virilis produces almost equal numbers of lethal and viable mutations.

SUMMARY AND CONCLUSIONS

1. Production of various X chromosome alterations has been studied in *Drosophila virilis* by treating mature sperm in males with about 3000 r units and mating them to homozygous marked females. A total of 83,949 F_1 females were examined.

2. The occurrence of F_1 females showing the different marker genes was found to vary. *Singed* occurred most frequently, with a rate of 0.0667 percent, and *crossveinless* occurred with the lowest rate.

3. When the F_1 females bearing the phenotypic expression of one of the marked loci were backcrossed the results varied from one locus to another. The F_1 females were divided into three groups, depending upon the results of this backcross: (1) undetermined due to sterility, (2) viable mutations, and (3) deletions or mutations that were lethal when hemizygous.

The frequency with which a particular locus produced each of the three classes was found to be independent of the frequency with which it produced the other classes. The *white* locus produced the highest rate of viable mutations and a low rate of lethals. The *apricot* locus produced the highest rate of deletions or lethals and ranked second in the rate of viable mutation and total frequency.

Changes at the singed locus most frequently resulted in sterile F_1 females and ranked third in visible mutations.

4. Non-disjunction males and females were obtained, but due to the method by which this experiment was conducted the results are not comparable to other published work.

5. Numerous hyperploid males were found. Thirty-seven had the same phenotype and one a different phenotype. The extent of the left end of the X chromosome which may be duplicated in a male without causing death seems to be from just to the right of echinus to the left end.

6. Thirty gynandromorphs and twenty-four mosaics produced are described. All of the mosaics from which the altered wild type chromosome was recovered were considered to be the result of a viable, point mutation either in one strand of a mature sperm chromosome or at the first cleavage division. One individual showed the effects of such a mutation in three-fourths of its body surface area. This is thought to be due to an unusual distribution of the cells to the imaginal discs. Two gynandromorphs which were three-fourths males may have been the result of the same unusual distribution or due to the loss of the paternal X chromosome in two successive mitotic divisions. All other gynandromorphs could be explained by a single loss at the first or later division. Male tissue occurred

more frequently in the head region than in the abdomen and probably more extensively on the dorsal side than on the ventral surface.

When the virilis gynandromorphs and mosaics, illustrated in the appendix, are compared to similar diagrams for melanogaster (Patterson and Stone 1938), those for virilis seem to possess more irregular patterns of male and female tissues. Numerous patches of female tissue are surrounded completely by male tissue and many segments derived from one imaginal disc contain tissue of both sexes. A possible explanation of this irregularity is that the distribution of male and female nuclei in the ectoderm from which the imaginal discs are formed is more random in virilis than in melanogaster.

7. One yellow mottled fly was produced as the result of a mutual translocation of the left tip of the X chromosome carrying the yellow locus and most of the sixth chromosome but not including the glossy locus. The yellow mottling seems to be due to a position effect of the yellow locus. The scute locus is also affected. Addition of a Y chromosome in the females does not seem to affect the mottling.

8. Drosophila virilis was found to produce viable, visible mutations slightly less frequently than Drosophila melanogaster when compared with available data for the yellow and white loci. Environmental conditions of the

different experiments may have influenced the frequency of mutation somewhat.

9. The ratio of viable to lethal mutations produced in virilis is almost one to one. This is strikingly different from the case of melanogaster where lethals are produced three to seven times as frequently as viable mutations. No single locus in melanogaster produced viable mutations more frequently than lethals whereas, several loci in virilis did produce significantly more viable than lethal mutations.

10. The production of mosaics and mottles is much more infrequent in virilis than in melanogaster.

11. No dominant mutations were found which would live homozygous except for a few which were inseparable from translocations.

Table 1

Test of proportion of mutations in relation to time after treatment.

Time of laying after treatment	Number bearing treated sperm	Number showing marker genes	Gynandromorphs and hyperploids	Total
0-2 days	7534	15	8	23
2-4 days	6502	13	8	21
4-5 days	5765	12	5	17

Table 2

Tabulation of F_1 mutations at marked loci.

Locus	F_1 females observed	Total mutations in F_1 ♀ number	%	Deletions or lethals number	%	Viable mutations number	%	Undetermined
y	83,949	13	0.0155	1	0.0012	11	0.013	1
cv	58,525	9	0.0154	3	0.005	1	0.0017	5
v	56,525	12	0.0212	2	0.0035	6	0.011	4
si	83,949	56	0.0667	16	0.019	13	0.015	27
dy	83,949	16	0.0191	4	0.0048	5	0.006	7
w	20,744	8	0.0386	1	0.0048	7	0.033	0
ap	66,525	38	0.0571	17	0.026	11	0.017	10

Table 3

Tabulation of non-disjunction, gynandromorphs, hyperploids, mosaics, and mottles.

	F_1 females observed	Number of occurrences	% of occurrence	Number producing offspring
Non-disjunction ♂	83,949	8	0.0095	2
Non-disjunction ♀	"	16	0.019	10
Gynandromorphs	"	30	0.035	7
Hyperploid ♂	"	38	0.045	0
Mosaics	"	24	0.029	20
Mottles	"	1	---	1

Table 4

F_1 mosaics and results when backcrossed.

Locus	Crossing-over	F_2 wild type ♀	F_2 wild type ♂	F_2 mutant ♀	F_2 mutant ♂	Remarks
y-1	normal	37	32	36	39	mosaic not y^{40} new allel not recovered
y-2	normal	0	0	125	104	50% y+; 50% y ec
y-3	normal	0	0	57	60	50% y+; 50% y ec
y-4	normal	12	9	27	33	22 y+; 38 y ec
y-5	normal	29	37	30	29	4 y+
y-6	normal	53	56	49	52	5 y+
y-7	normal	42	36	39	43	no class of y+
y-8	normal	20	25	13	15	no class of y+
si-9	normal	0	0	61	61	46 +si+
si-10	normal	2	3	58	56	34 +si+
si-11	normal	0	0	18	15	50% +si+
si-12	normal	85	1	48	42	2 +si+
si-13	---	0	1	0	5	
si-14	---	--	--	--	--	sterile
si-15	---	1	0	1	5	F_2 ♀ sterile
si-16	---	--	--	--	--	sterile
dy-17-24	normal					mutated chromosome not recov.

Table 5

Comparison of viable and lethal mutations in D. melanogaster from Patterson's data and D. virilis. Loci may be compared vertically by ratios only. See text.
M=melanogaster; V= virilis; y=yellow; w=white; cv=crossveinless; sn=singed; si=singed; v=vermilion; g=garnet; ap=apricot; wN=white, notched.

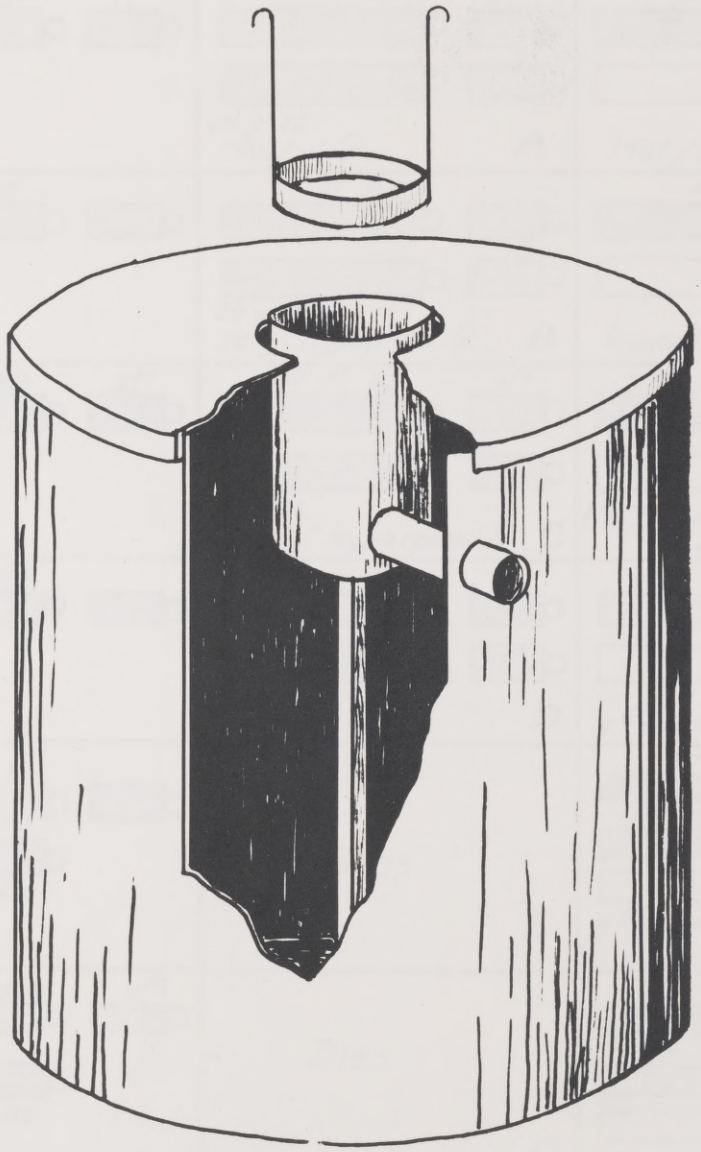
	M y	V y	M w	M wN	V w	M cv	V cv	M sn	V si	M v	V v	M g	V ap	Total M	Total V	Total for M 14 genes	Total for V 7 genes	Mottles M	Mottles V
Lethals and/or deletions	16	1	20	21	1	3	3	0	16	2	2	4	17	63	40	112	44		
Point mutations	2	11	4	0	7	0	1	0	13	0	6	3	11	9	49	16	54		
Undetermined	12	1	10	10	0	0	5	3	27	3	4	1	10	39	47	102	54		
Total	30	13	34/65	31	8	3	9	3	56	5	12	8	38	111	136	230	152	32w	1y

Table 6

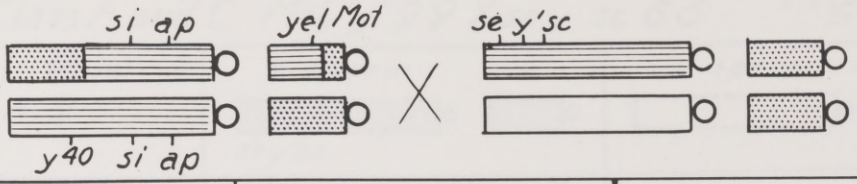
Comparison of viable and lethal mutations in D. melanogaster from Demerec's data and D. virilis. Loci may be compared by the ratio of the classes in the vertical columns. See text. M=melanogaster; V=virilis; w=white; dy=dusky; g=garnet; ap=apricot.

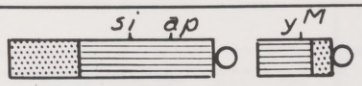
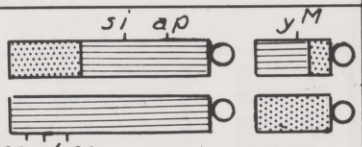
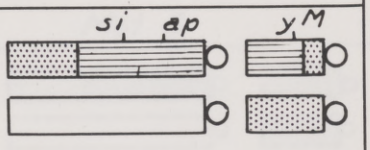
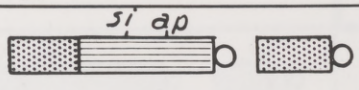
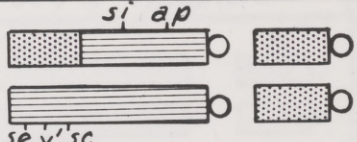
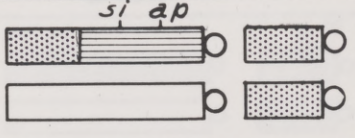
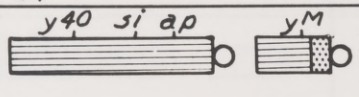
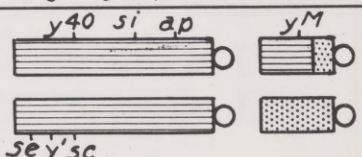
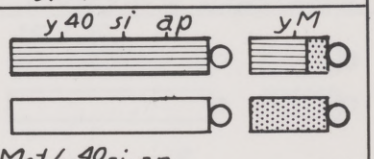
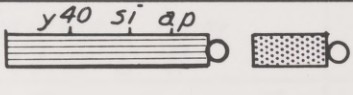
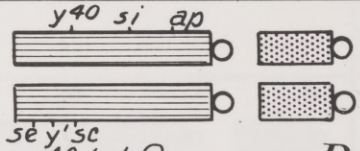
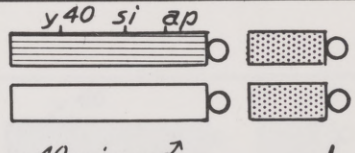
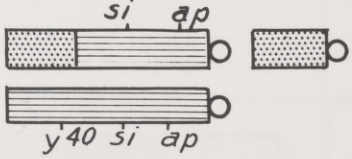
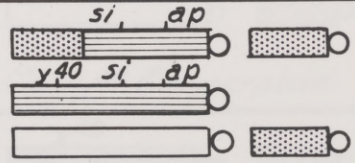
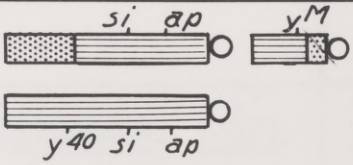
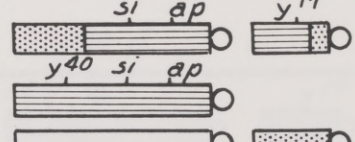
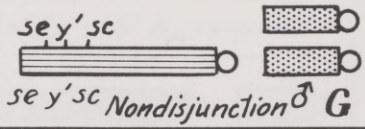
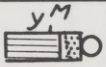
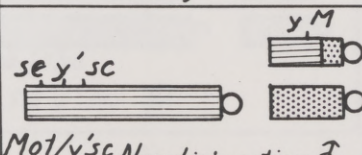
	M w	V w	M dy	V dy	M g	V ap	Total M	Total V	Total for M 5 genes	Total for V 8 genes
Lethal	7	1	5	4	3	17	15	22	34	44
Viable mutations	4	7	0	5	1	11	5	23	15	54
Undetermined	0	0	1	7	0	10	1	17	2	54
Total	11	8	6	16	4	38	21	62	51	152

Fig. 1



Mot y40 si ap ♀ X se y' sc ♂ Fig. 2



Female gametes	se y' sc X sperm	Y sperm
Type 1 	 se y' sc Mot/y' ♀ A	 Mot/si ap ♂ I
Type 2 	 se y' sc se y' hypoploid ♀ B	 hypoploid ♂ Dies J
Type 3 	 se y' sc Mot/y' hyperploid ♀ C	 Mot/y40si ap hyperploid ♂ K
Type 4 	 se y' sc y40/y' ♀ D	 y40 si ap ♂ L
Type 5 	Dies E	 y40si ap xxy ♀ hypoploid M
Type 6 Nondisjunction 	Dies F	 Mot/y40 si ap ♀ N
Type 7 Nondisjunction 	 se y' sc Nondisjunction ♂ G	Dies O
Type 8 	 Mot/y' sc Nondisjunction ♂ H	Dies P

Class A and C Mot/y' ♀♀ X se y' sc ♂♂ Fig. 3

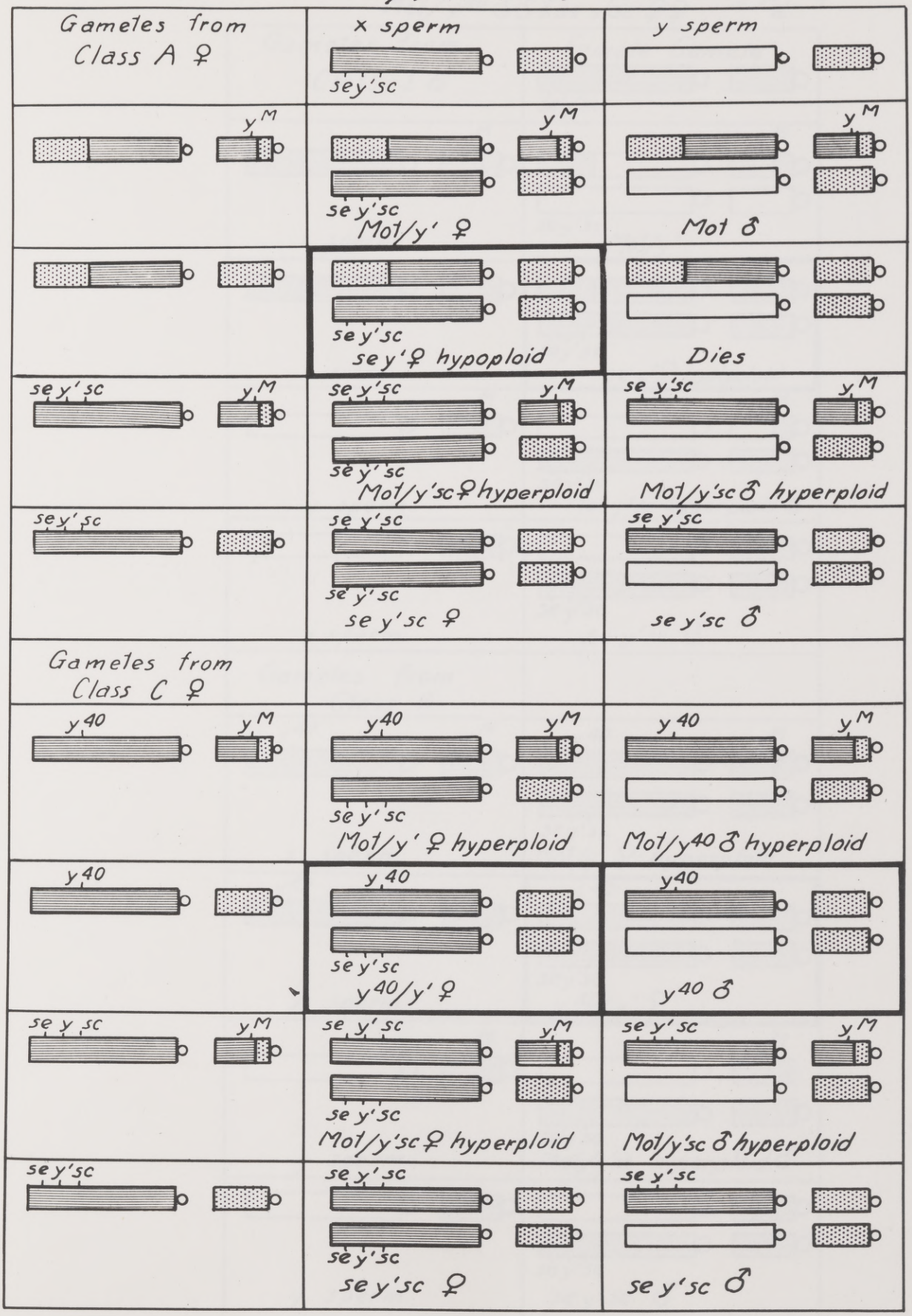
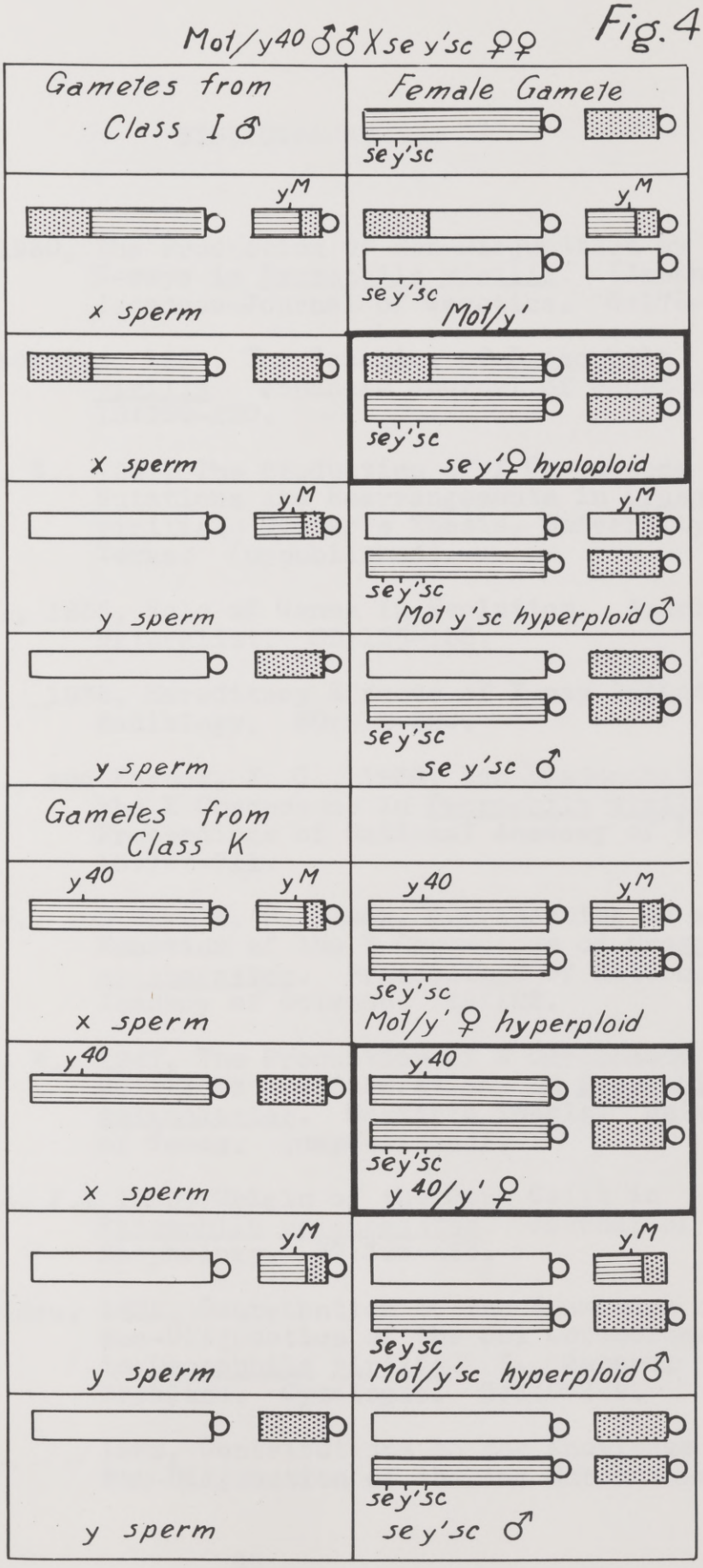


Fig. 4


Mot/y40 ♂♂ X se y'sc ♀♀
Gametes from Class I ♂
Female Gamete
se y'sc
yM
x sperm
Mot/y'
sey'♀ hyploploid
y sperm
Mot y'sc hyperploid ♂
se y'sc ♂
Gametes from Class K
y40
Mot/y' ♀ hyperploid
y 40/y' ♀
seysc
Mot/y'sc hyperploid ♂

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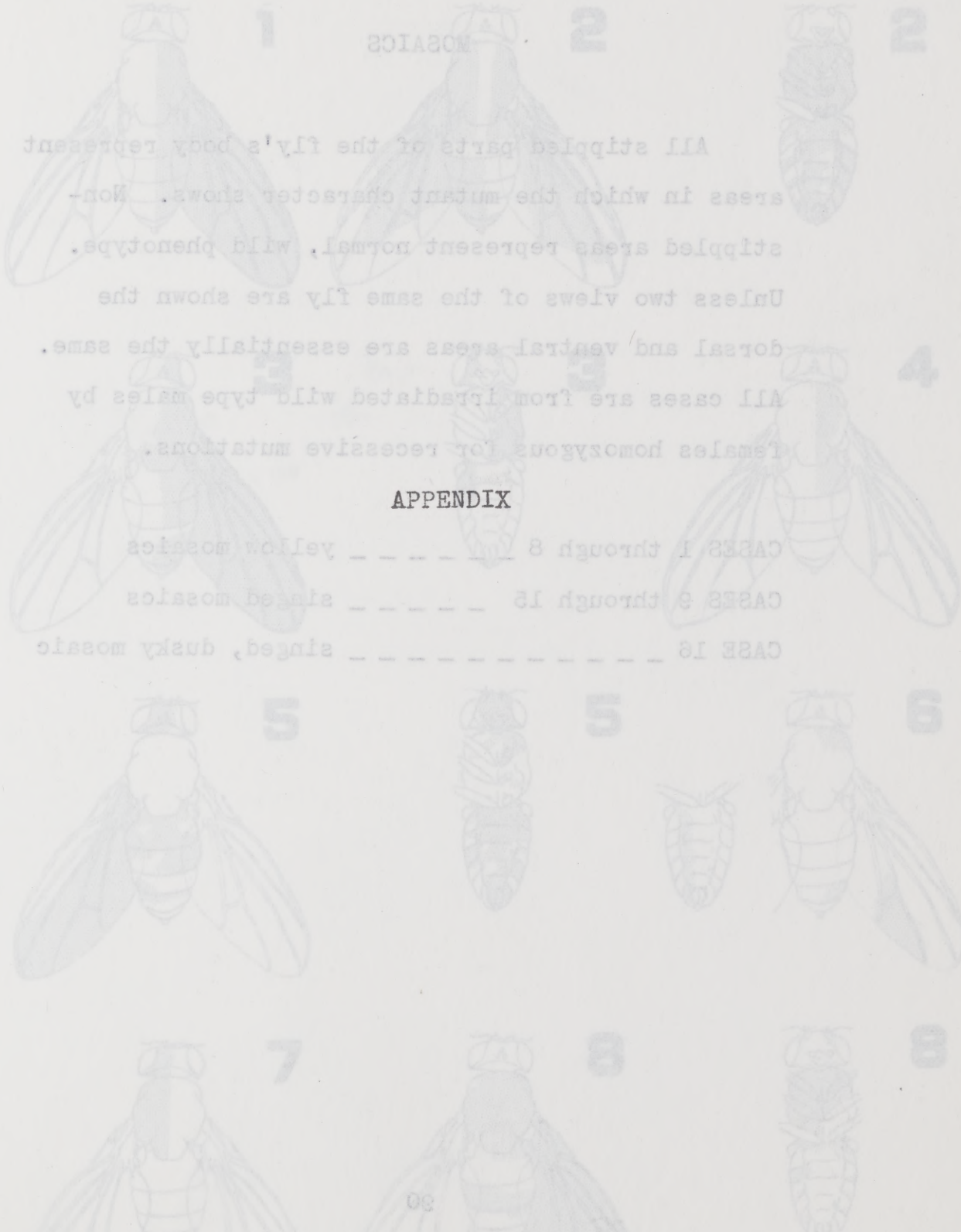
APPENDIX

PLATE I



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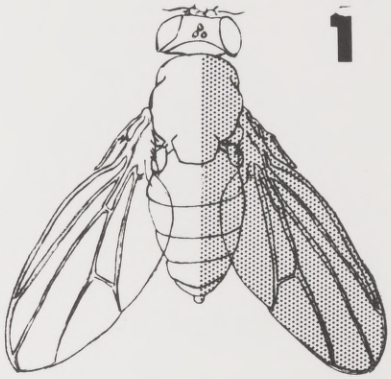
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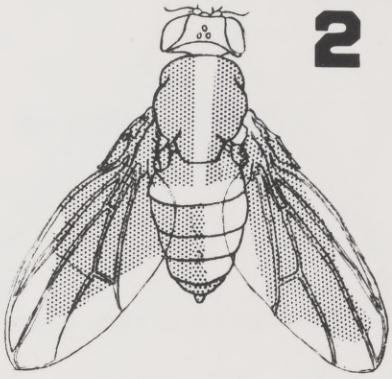
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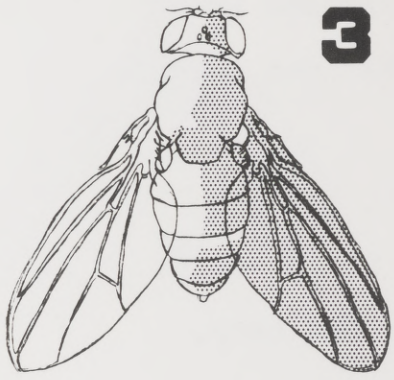
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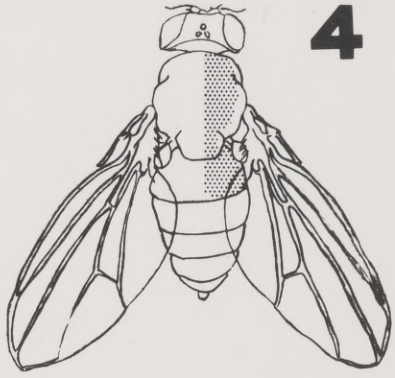
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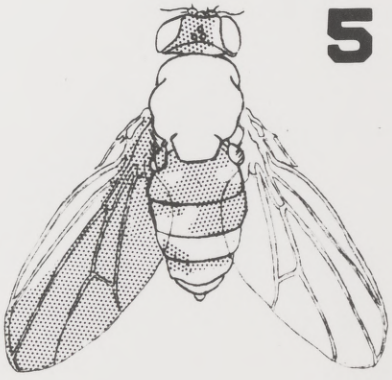
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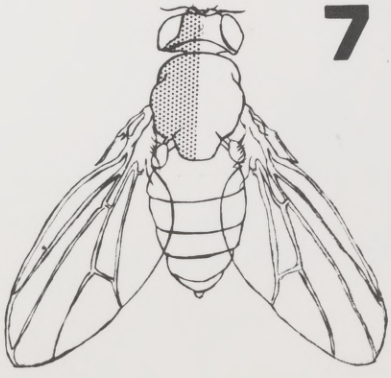
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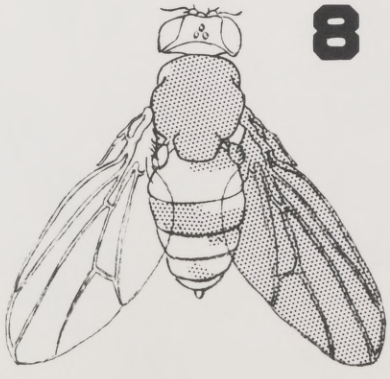
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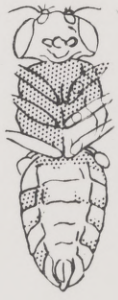
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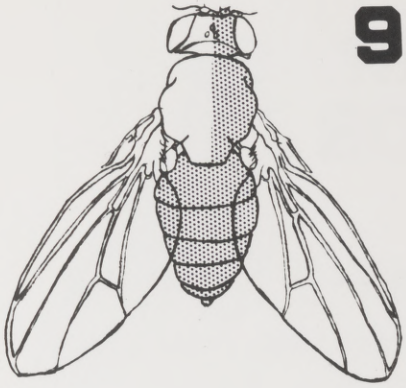

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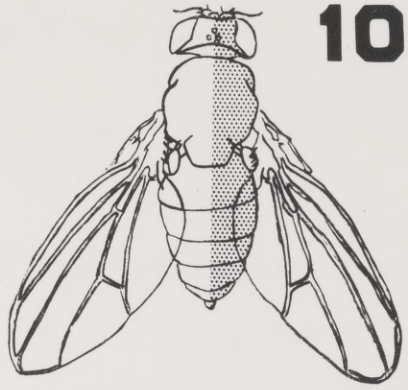

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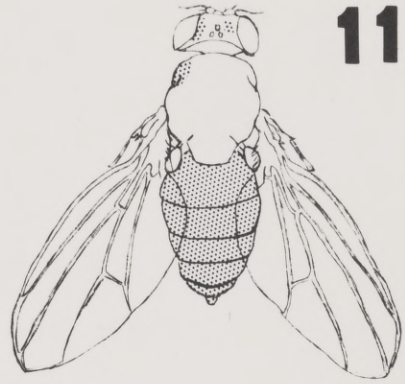

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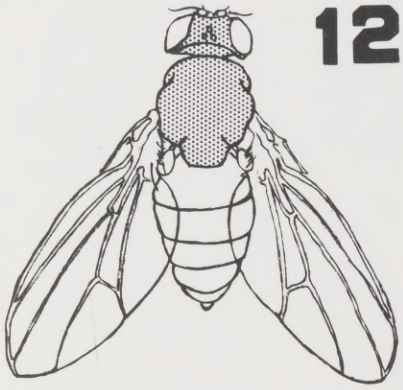

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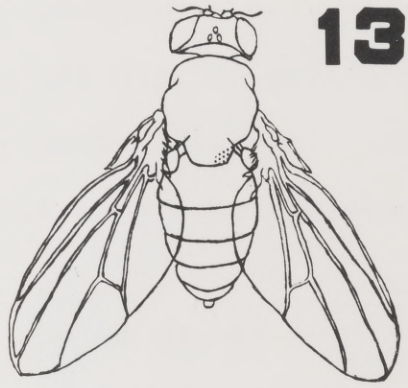

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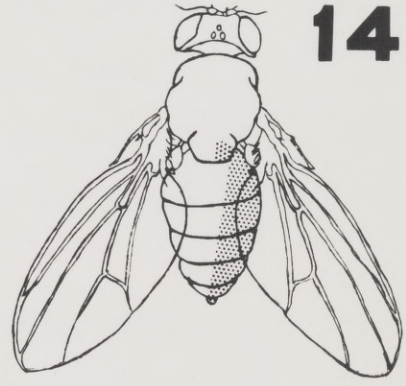

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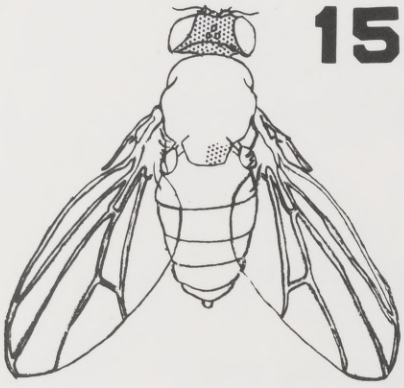

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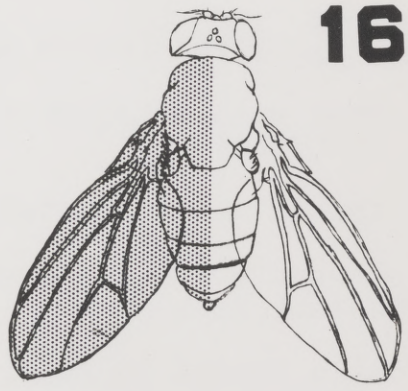

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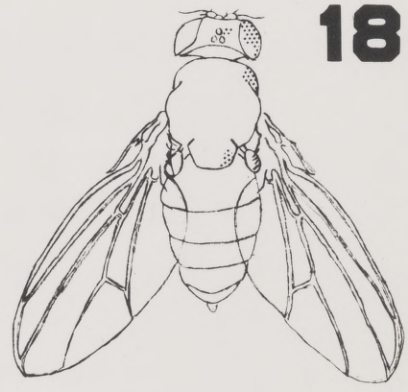

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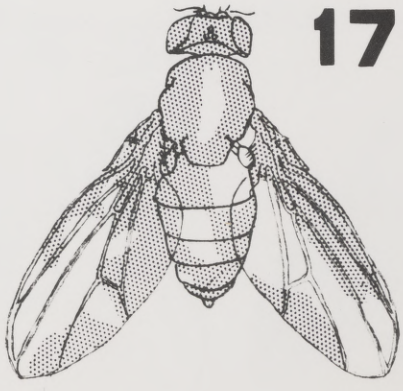

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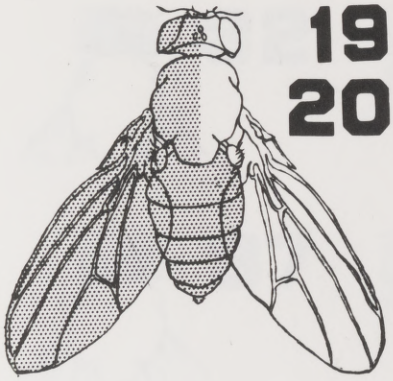

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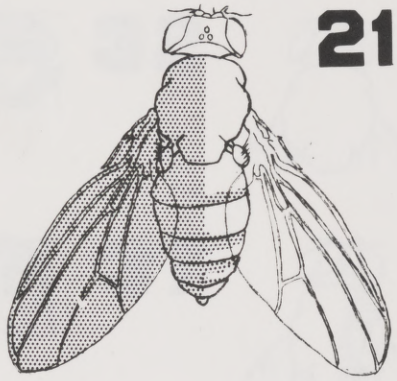

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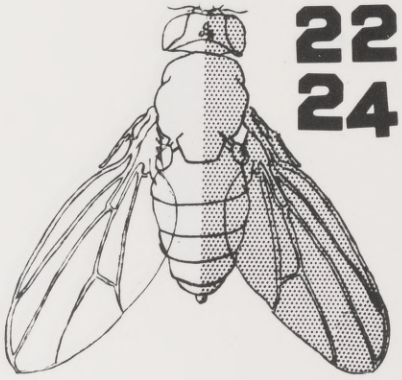

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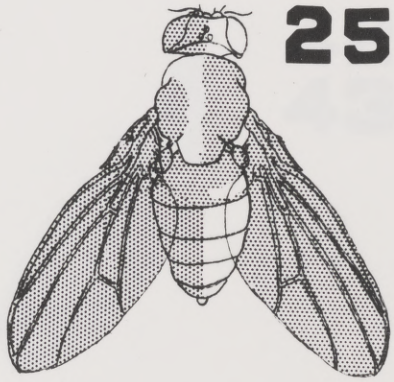

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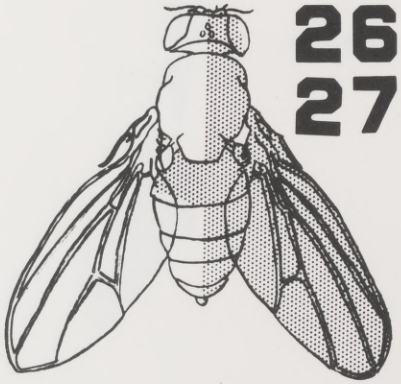

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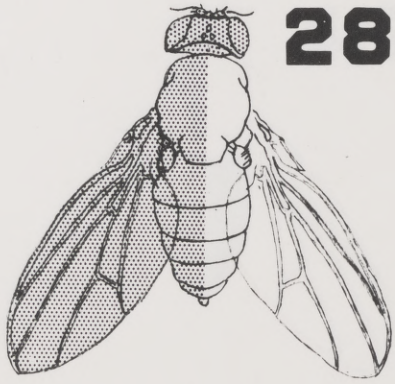

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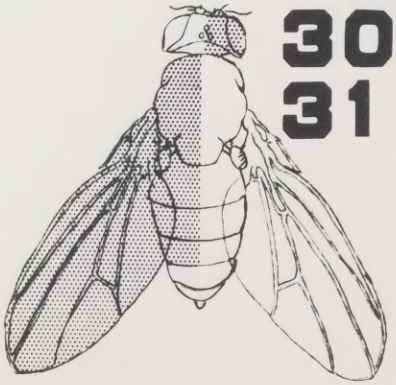

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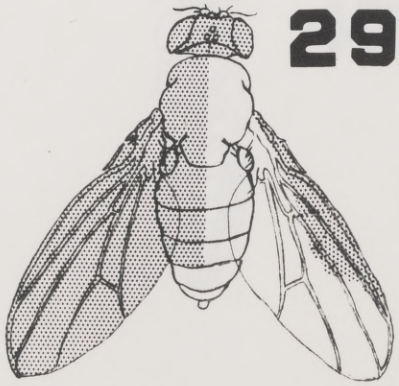

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PLATE IV

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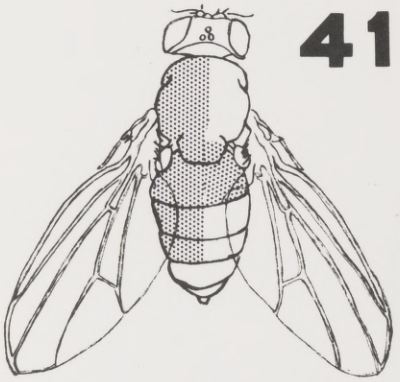

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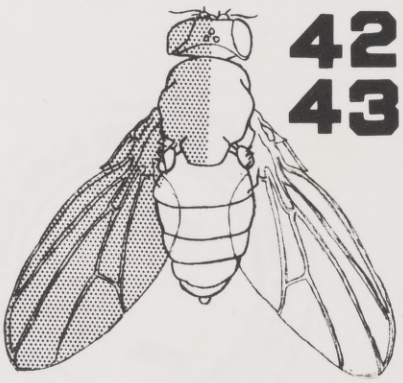

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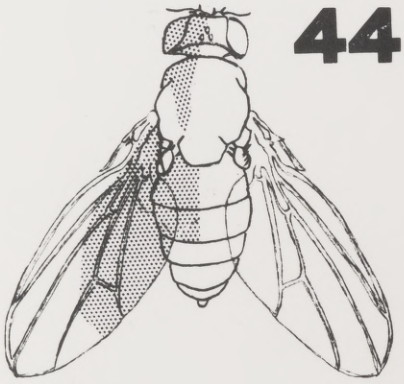

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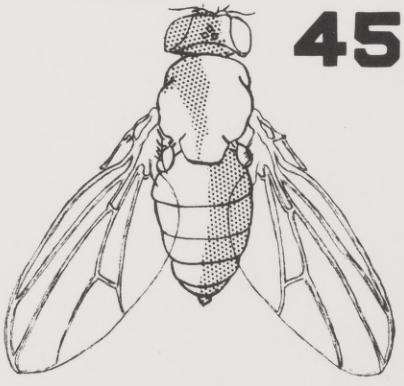

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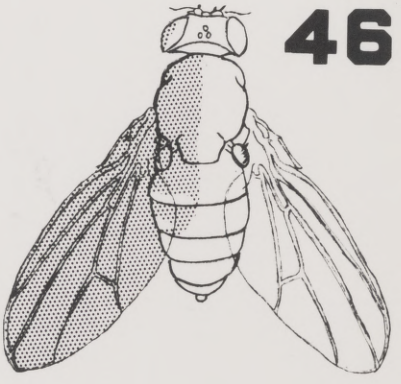

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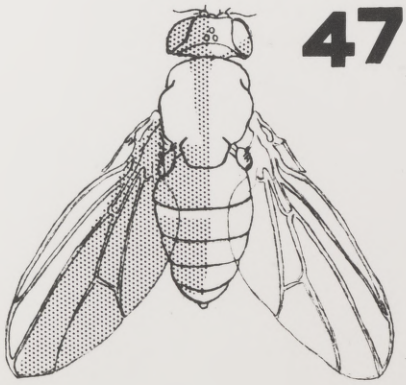

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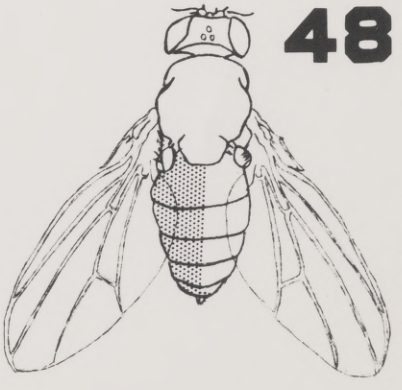

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